NATURE

A Weekly Journal of Science

Vol. 190, No. 4773 SATURDAY, APRIL 22, 1961 2s. 6d.

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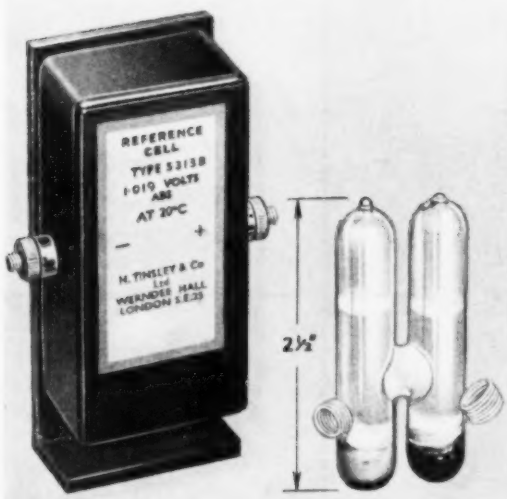

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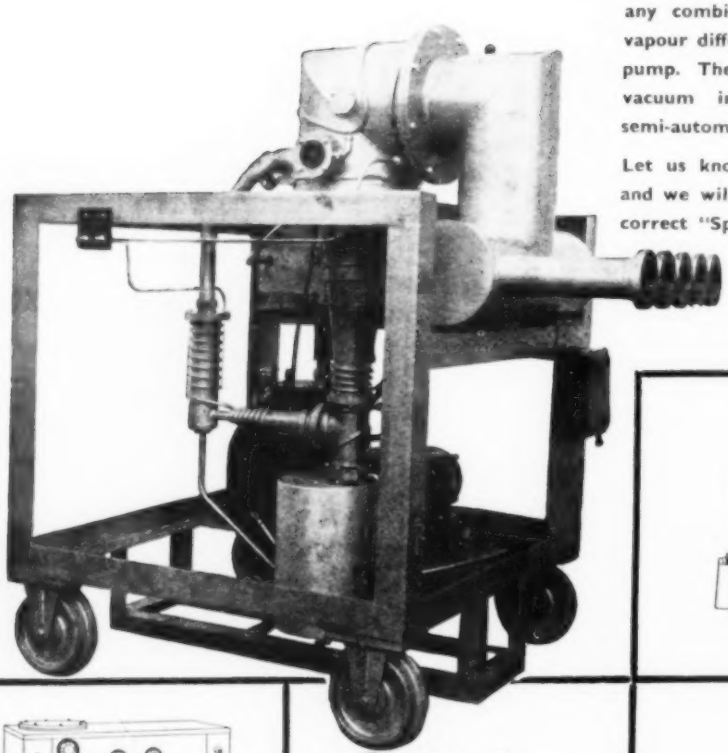

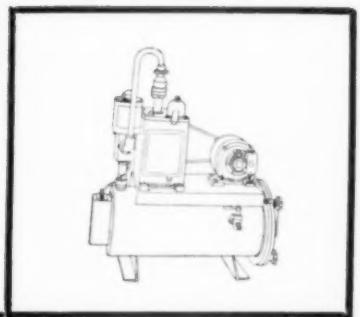

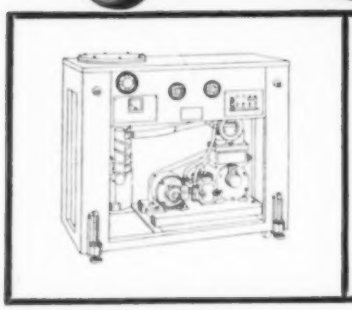

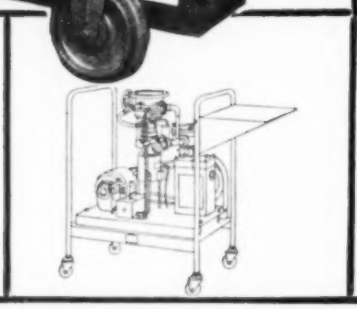

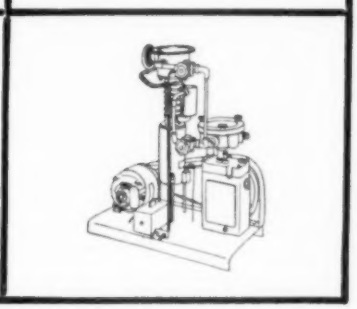

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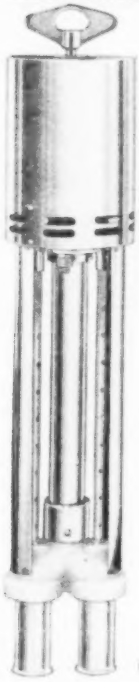

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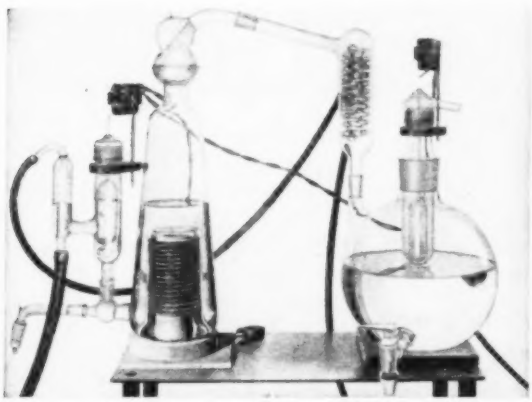

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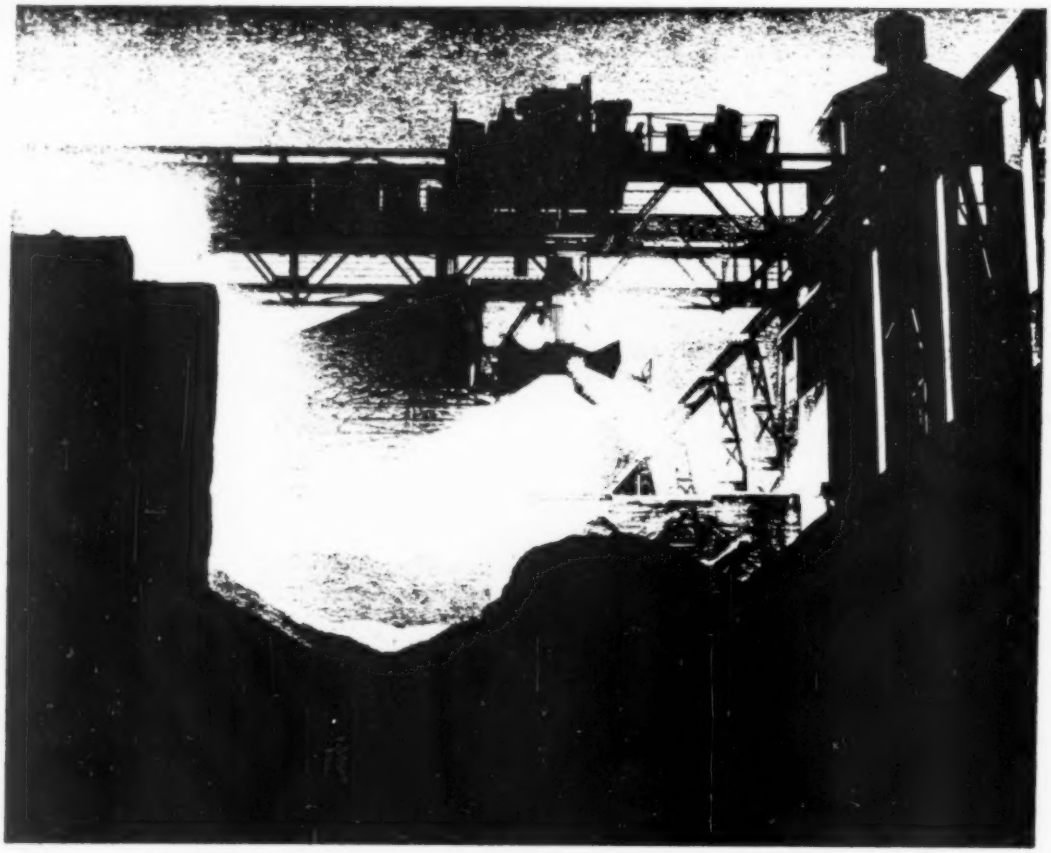

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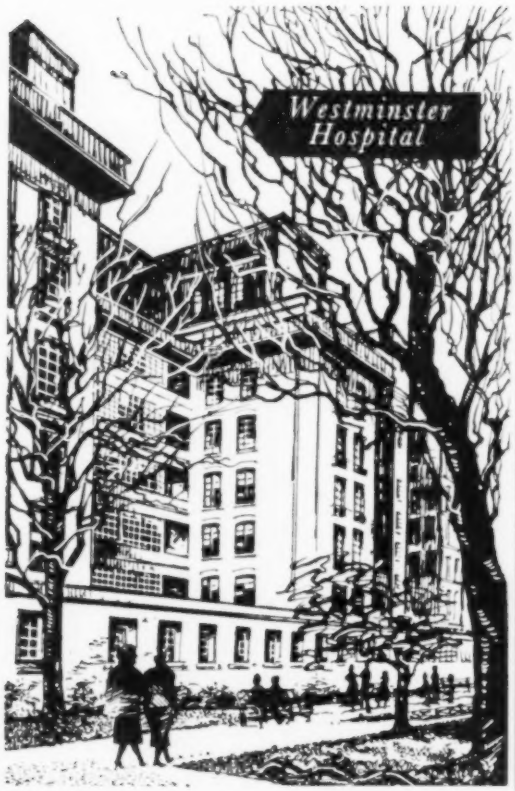

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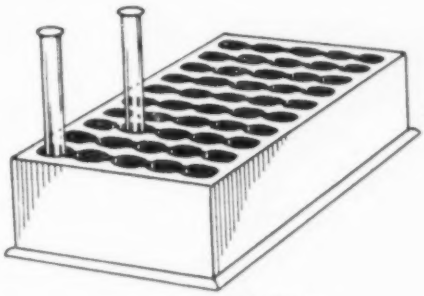

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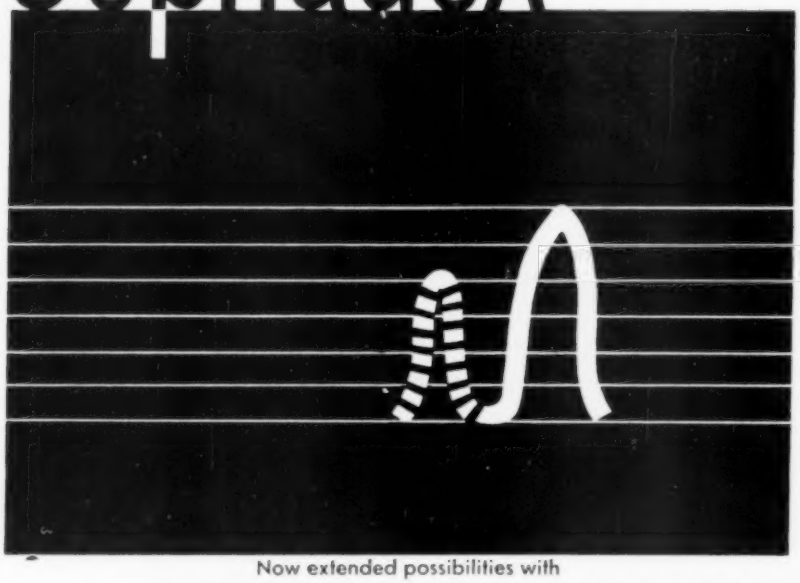

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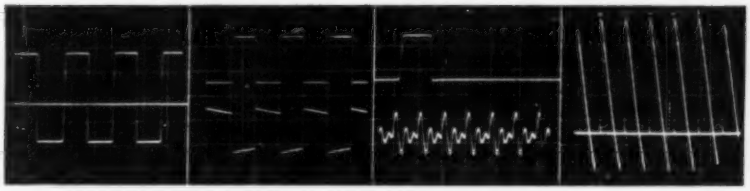

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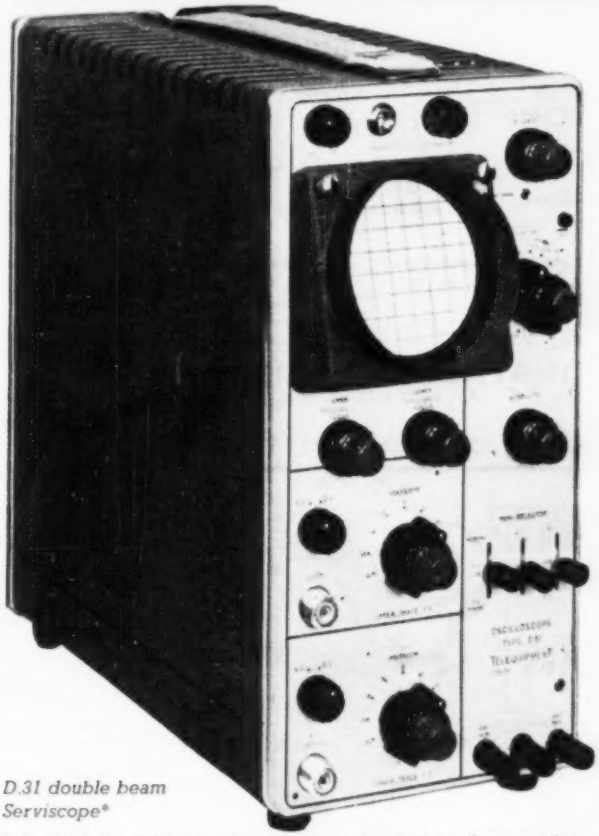

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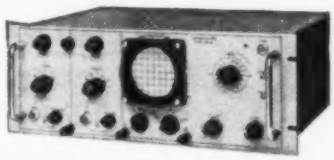

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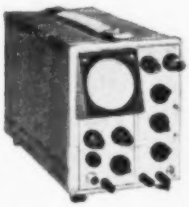

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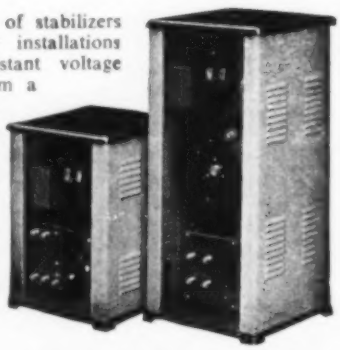

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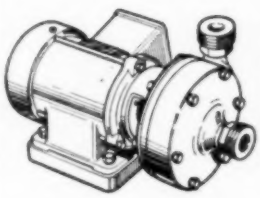

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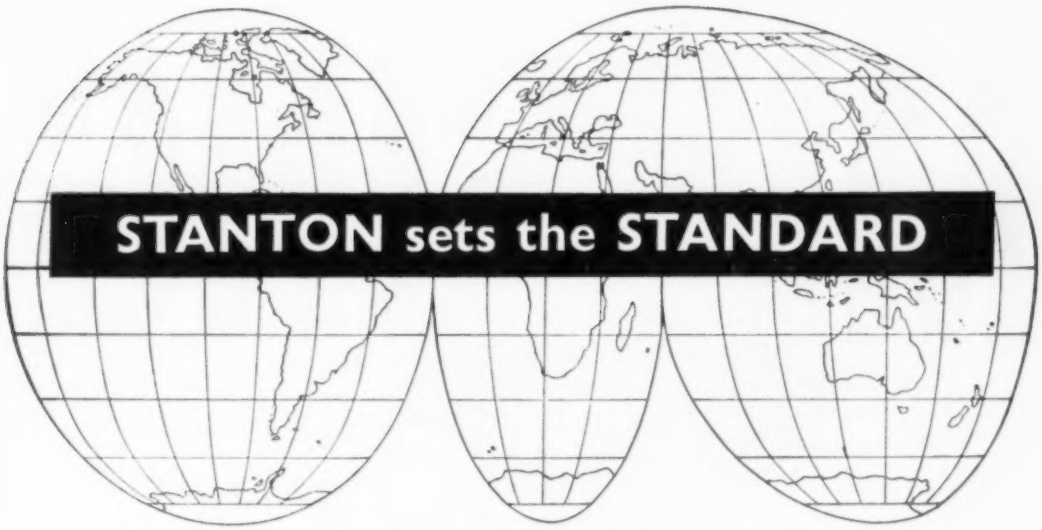

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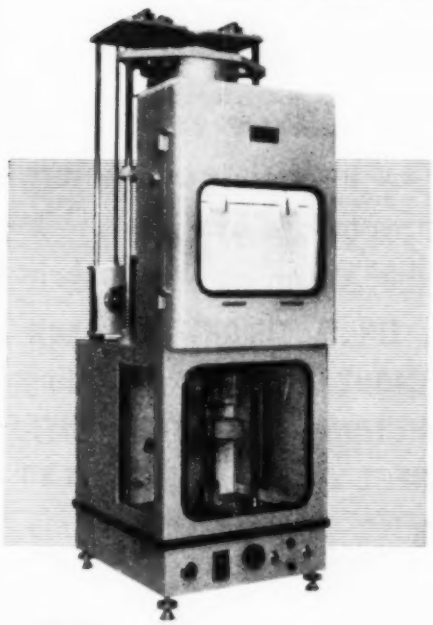

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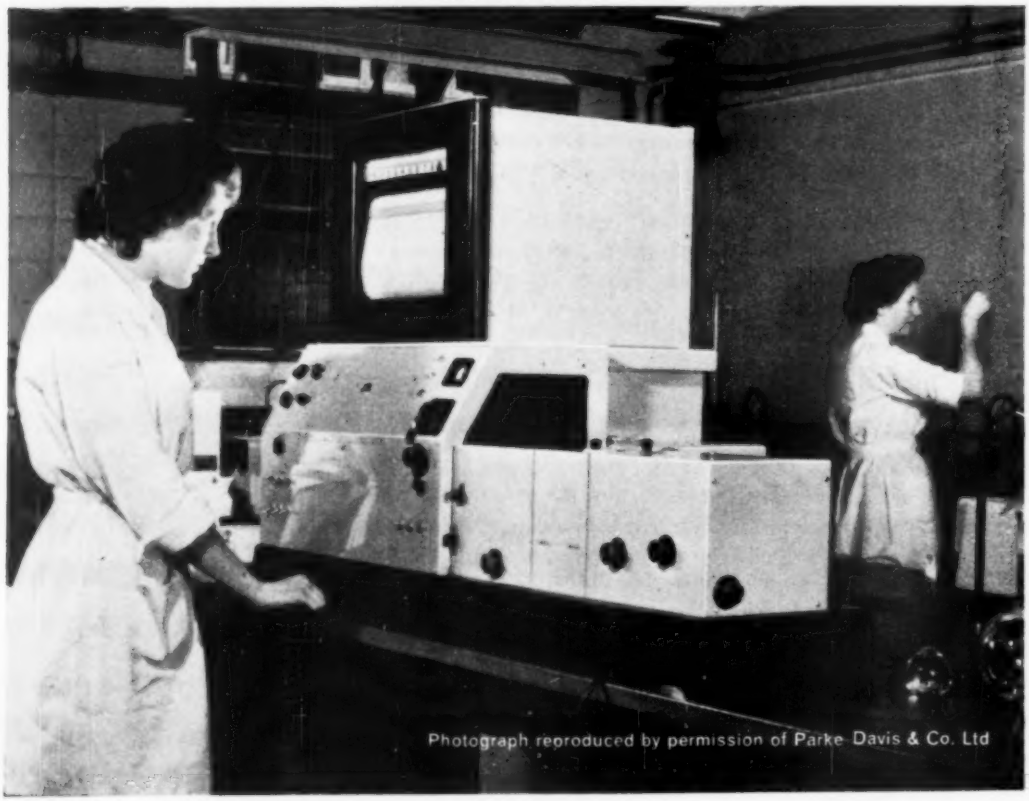

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A TRIUMPH FOR SCIENCE

IN *Nature* of October 12, 1957, p. 719, we were glad and proud to congratulate the scientists and technologists of the U.S.S.R. on the successful launching of the first artificial Earth satellite (*Sputnik I*). Less than a month afterwards (*Nature*, 180, 931; 1957), we again had occasion to congratulate the U.S.S.R., when the second satellite (*Sputnik II*) was launched, this time containing a dog. Though both these satellites eventually disintegrated in space, enough evidence had been obtained, especially from *Sputnik II*, to indicate that it was possible for living things (even mammals) to withstand the strain of being launched into orbit. Since then, Russian, American and other scientists have made astounding progress in space research using rockets, satellites, etc. Two more recent achievements, perhaps most important of all, were the placing into orbit of satellites containing dogs and recovering them with the dogs alive. This was done by scientists in the U.S.S.R. on August 16, 1960, and again on March 9 of this year.

The significance of these great achievements, all made so recently as during the past four years, needs no stressing now; but one cannot refrain from expressing concern that though each achievement has deservedly received world-wide acclaim, the science and technology behind each are, by and large, known only to the chosen few.

Now again, on April 12, a still further point in scientific advancement was reached, for on that day scientists and technologists in the U.S.S.R. reaped a rich reward for concentrated and ingenious research by successfully launching another space-vehicle (*Vostok*) into space. This satellite carried, among other things, a man (Major Yuri Alekseyevich Gagarin), travelled in orbit around the Earth in 89 min. 6 sec., and a little later was brought back safely to Earth, with Major Gagarin unharmed—all in about 108 min. Moreover, the Russians claim that every part of the space-vehicle was recovered intact and can be used again. (See also p. 307 of this issue.)

The entire world, scientists and non-scientists alike, has learned of this great feat with awe and admiration, and we hasten to praise and congratulate the scientists and technologists who were responsible. Moreover, Major Gagarin is to be commended on his courage and devotion to duty.

It seems timely, therefore, once again to emphasize what we consider to be the true significance of the magnificent results obtained in space research by Russian, American and, indeed, other men of science. We may ask: Are these great feats being worked for, paid heavily for and finally achieved amidst world applause mainly for political prestige or military advantage, or for the advancement of science in its truest sense, that is, the enhancement of man and his culture? There is certainly no gainsaying the scientific results, for they are there for all to see; and the scientists and technologists concerned (most of them, apart from Kapitza, Sedov and Blagonravov, for example, unknown outside the U.S.S.R.) are, it is assumed, being awarded their just honours and dues. But the time has long since passed when the scientist either need not or does not concern himself with the consequence of his work; so the most important question now is: How are these magnificent scientific achievements to be utilized in the near and distant future? Quite rightly, we think, the scientist himself should not be the sole arbiter in this problem. But it is for everyone to see that the right people make the right decisions for the sake of world progress and peace. We are often being told that it is the people of a nation and the peoples of the world who decide policy and make final decisions, and that their so-called leaders, especially in the political arena, are not really their leaders but actually their servants. If this is the case, then the world community must see that scientific results are used wisely; but the community can do so only if it has a true understanding and appreciation of the significance and message of science.

But it is very doubtful if the layman really appreciates what is going on in the world of science to-day, despite the greater attempts at improving education both through specialized agencies such as universities and technical colleges and through mass media. Our formal academies of teaching and learning, such as schools and universities, cannot, by themselves, prepare the ground for the most desirable growth, development, appreciation and application of the new knowledge. Neither will the plausible projects of increasing the number of universities and technical colleges solve the problem; they can only scratch the surface.

There are other means of education, equally important, albeit mainly mass education—television, sound broadcasting, the cinema, books and, above all, the newspaper Press; but, alas, all too often these soon become reduced to arenas for political propaganda.

Ignorance provides the most fertile ground for undesirable propaganda of all sorts, especially politics. So to what extent does the Press attempt to give science its fair due, and thus lay the foundation for creating the type of mind that can assess wisely the value of any form of scientific achievement, whether it be in space research or antibiotics? It is very significant, alarmingly so, in fact, that the Press seems to have developed a poor sense of values, and preys on the weakness and foibles of human nature rather than attempts to stimulate the interest of its readers in things of greater moment and of inestimably more value to man and his cultural development. It is a sad reflexion that it takes a man travelling in orbit around the Earth to give science one of its all too few banner headlines in the newspapers. The same could be said of other aspects of cultural development which aims at international collaboration and peace. It is relevant here to refer to a recent American

survey which has shown that a certain film actress was mentioned more often than anyone else in the world in the daily newspapers of 1960.

Another comparison may not come amiss. A photograph of a section of a crowd in Moscow, taken just after the *Vostok* news was released, seemed reminiscent of a photograph of a crowd outside the entrance to a London hospital. But there was a difference, in that the former wore, with understandable justification, jubilant and happy expressions on their faces, whereas the latter seemed taut, anxious and expectant, for they were a crowd of Press photographers anxious to take photographs of visitors to another film actress lying ill in the hospital. The sense of values of both Press and public on the two sides of the Iron Curtain seems to be vastly different.

Many of the comments on the recent news from the U.S.S.R., at any rate in the British Press, betrays a deplorable lack among some writers of a true appreciation of the technique, aims and objectives of science. Moreover, a sense of proportion seems to be sacrificed to sensationalism. For example, one feature article is devoted entirely to urging Britain to award some form of honour to Major Gagarin. It is fairly certain that to bestow on Major Gagarin an honorary George Cross, in recognition of his courage and bravery, would meet with popular acclaim; but, alas, the article in question directs all its proposals to British scientific societies, including a suggestion that the Royal Society of London should consider conferring the great scientific distinction of foreign membership on the Major. We have no doubt that it can be left to the Royal Society to maintain its sense of proportion, and while, perhaps, officially congratulating the Academy of Sciences of the U.S.S.R., continue to confine its distinguished foreign membership to scientists who have personally made outstanding contributions to fundamental scientific knowledge.

Another writer refers to scientists as being the "most optimistic and dangerous men in the world". Men of science can ill afford to ignore such absurd suggestions and comments about themselves, in spite of the fact that most ill-informed statements concerning science appear in the so-called 'popular' newspapers. The fact that science is so misrepresented should give cause for grave concern, for it is such newspapers which enjoy the largest circulation and are therefore read by the majority of people.

The official announcement of Russia's recent great scientific victory reads (in part) as follows:

"We, *Soviet people building Communism* [italics ours] have had the honour of being the first to enter into outer space. The victories in the exploration of the cosmos are regarded by us as not only the achievement of our people but also of entire mankind.

"We gladly place them at the service of all peoples in the name of progress, happiness and the well-being of all human beings on earth. We do not place our achievements and discoveries at the service of war but at the service of peace and security of peoples.

"On this solemn day, we address once again the peoples and governments of all countries an appeal for peace. May all people, irrespective of race and nation, colour, religious beliefs and social condition, devote all their efforts to safe-guarding stable peace throughout the world".

This is a most noble statement. We, as scientists, subscribe wholeheartedly to it and to the jubilation of Soviet Russia; indeed, we feel we have a share in it. Science cannot recognize national frontiers. There is no such thing as Communist science, or American science or British science; there is just *Science*. Moreover, present-day science is built up on science of the past (Sir Isaac Newton contributed largely to this latest Russian victory, three hundred years ago); and present-day science is the basis for the science of the future. Science, like other cultures and disciplines, has been, is and will be in a state of evolution, and the pace of such evolution depends mainly on a host of genera and species of scientists, none of whom can afford to ignore the rest. While, therefore, reading with satisfaction the official Russian announcement, we think it is a pity that the words printed in italics were included. This great achievement is not a victory for Communism, any more than the great achievements in space research in America are a victory for democracy—in the political sense. All such achievements are the victories of science over Nature.

Conversely, it is equally disturbing to read that the news was received in the United States with "little surprise but deep disappointment", and that in Cape Canaveral a man working in the American space programme commented that the recent news from Russia "just makes me sick".

So, as a corollary, it is essential that we all realize that if the scientists and technologists do not get the sympathetic understanding and practical support they deserve, then those in political authority, coupled with their advisers, must accept the immediate blame; though the ultimate blame must rest on all those responsible for our education and for the mass dissemination and interpretation of knowledge.

One views with no little concern the utilization of science for political propaganda. The layman is not prepared for such news, and the majority of the public is in no position to evaluate the results. One otherwise quite intelligent person, on hearing the news, just commented: "I am now really afraid". It seems that the general public throughout the world is accepting as a fact that space research is now a race between Communists and the rest—mainly between the U.S.S.R. and the U.S.A. This cannot be a good omen for world peace, neither is it to the advantage of science in its dispassionate search for truth. The President of the United States has said that he is tired of being second in the space race with the U.S.S.R. Perhaps now, instead of making further efforts to become first, greater effort can be made by all the great Powers to arrange for a global pooling of scientific knowledge, thus forming the basis of H. G. Wells's ideal of a *World Encyclopædia*; but while there is so much political bad faith and open schism between countries, coupled with the hitherto tardy recognition that science is useful in peace as well

as in war, there seems to be little hope of such international collaboration. Moreover, it is futile to blame any one country for such refusal to collaborate, in spite of the fact that collaboration must be based on an all-or-none policy.

Despite the fact that the U.S.S.R. has been the first in some of the initial stages of space research (for there are undoubtedly many more stages to follow) it must be recognized that American contributions (though comparatively less spectacular and hence not having such 'hot' news or political propaganda value) to this now fashionable aspect of scientific research are by no means, therefore, of secondary importance. In fact, during these initial years, even if all data and results could be duly weighed and evaluated, it would be difficult to say which of these great Powers has contributed most, so far, to our knowledge of terrestrial and extra-terrestrial science; and since no one authority is in possession of all the facts it is virtually impossible to say which, from the scientific point of view, has done most towards the establishment and development of space research. Yet, in the long (perhaps very long) run, it will be the scientific assessment which really counts.

The kind of scientific competition, both inter- and intra-national, that we are experiencing to-day cannot be a healthy one. Claims for priority sometimes become quite nauseating. It is all bound to lead to misrepresentation, exaggeration, unfair claims, secrecy and consequently suspicion, and altogether general misunderstanding especially among the general public; and this provides fertile ground for political propaganda of the worst kind. (The Russian reports of even this latest feat are somewhat contradictory, and this has immediately had the effect among some people of querying the facts or wondering if some ancillary statements have been made deliberately to confuse the issue among other scientists of the world.) Apart from this, secrecy and surreptitious competition must involve wasteful and very expensive duplication of effort. Gone are the days when one could speak with pride, and justifiably take for granted, freedom in science; that is, freedom in research, freedom in discussion and debate, and above all freedom in exposition to the entire world of new scientific findings.

Lord Hailsham, the British Minister for Science, has said that it would be better and more economical to conduct inquiries concerning the Universe on an international basis. Most scientists, including, we think, many in the U.S.S.R., will subscribe to this view. But, as pointed out by Lord Hailsham, British development of full-scale manned space flight would be a misuse of scarce man-power and economic effort. We trust this will not be interpreted as a scientific dichotomy of the nations of the world into the 'haves' and 'have-nots', for that would be following the absurd propaganda of Nazi Germany. Rather would we accept Lord Hailsham's views and couple them with those of Mr. Harold Macmillan, who recently emphasized that scientific research is not confined to that of 'space'. In all branches of scientific research, for centuries, Britain has contributed its share—in some cases the lion's share; and history frequently puts Britain in the vanguard. Moreover, the urge among scientists to collaborate with each other, irrespective of nationality, is continually being emphasized by the large number of international scientific conferences held in many parts of the world.

Nevertheless, one must realize that the 'Iron Curtain' exists, even for scientists; and while that is allowed to continue to affect science, the humanities and other branches of cultural development there is bound to be a threat to the dignity of man and his very destiny.

It was Herbert Spencer who said that: "Science is organized knowledge". To-day, science has evolved well beyond that definition. However, even if we are prepared, in principle, to accept Spencer's aphorism we should modify it to read 'card indexed' rather than "organized". But, alas, the index cards are not all in the same file to which the entire scientific world may add and/or refer.

This makes all the more relevant and significant the comment made by Sir Bernard Lovell, director of the Jodrell Bank Experimental Station, when referring to this, the latest and greatest triumph of the scientists in the U.S.S.R.

"I think it is remarkable that a nation which was largely illiterate only a generation ago has succeeded in this immense task. It has done this because of the singleness of purpose and human sacrifice in material comforts on a scale unknown in the West.

"If the Western civilizations continue to disregard this example of the great results of investment in science, education and research, they will do so at their peril".

We do not advocate copying the methods in education being adopted in the U.S.S.R.; but we would urge that peoples of the world take note of this recent evidence of the result of encouraging science and scientists. That is best done, fundamentally, by giving sound scientific education to all, so that scientists will receive the encouragement they now lack, and when new scientific results are announced, the non-scientists (very much in the majority, and some in powerful authority) will, in consultation with the scientists themselves, take enthusiastic and intelligent note and be in a position to assess wisely and decide sensibly how such results shall be applied to the advancement of mankind.

At present, we seem to be paying only lip-service to the ideal that scientific achievements should transcend all political and racial barriers. For example, on several occasions during recent years, *Nature* has tried, through personnel of the Moscow Academy of Sciences, to persuade scientists of the U.S.S.R. not to persist in hiding their light under a bushel. But either they or their political superiors have so far turned deaf ears to such appeals. If the time does come when we have achieved that ideal, then shall we be able to congratulate those responsible for any notable scientific feat *because they are scientists*, not because they are members of any one nation or subscribers to any particular political creed.

A TREATISE ON ANALYTICAL CHEMISTRY

Comprehensive Analytical Chemistry

Edited by Prof. Cecil L. Wilson and David W. Wilson. Vol. 1*B*: Classical Analysis. Pp. xxii+878. (Amsterdam: Elsevier Publishing Company; London: D. Van Nostrand Company, Ltd., 1960.) 155*s*.

THIS book, Vol. 1*B*, comprises the second part of the first volume of this series on "Comprehensive Analytical Chemistry" which is being produced under the direction of an advisory board of acknowledged world experts in the various fields of analysis. This monumental scientific work is edited by Prof. C. L. Wilson and his brother, D. W. Wilson, both of whom are particularly eminent as microchemists and as teachers of the analytical method.

The first volume, 1*A*, has already received much well-merited eulogistic comment from readers and reviewers, and this second volume, dealing with classical methods of inorganic titrimetric and organic quantitative analysis, is also an extensive and scientifically detailed publication of the highest standard. The text is lucidly annotated where necessary and the reference bibliographies to each section are both helpful and comprehensive. The construction of laboratory apparatus is illustrated with great diagrammatic clarity, and the numerical tables and graphical representations form a most useful supplement to the text.

The theoretical and thermodynamical principles governing the analytical procedures are presented in much detail, and the academic student will welcome those extensive sections dealing with complexans, redox potentials, ionic equilibria, etc.

Much practical laboratory detail is also included in those descriptive parts relating to reagents, apparatus, methods, etc.; this makes the book singularly attractive to the young chemical analyst, who will find a wealth of experience and sound advice presented in a most assimilable manner. For the more mature analyst, there are descriptions of the recent modern techniques, of reagent standards, chelate compounds, a very extensive section on complexan reactions and titrimetry, potentiometric and amperometric methods, etc. The inorganic sections covers every titrimetric reagent normally used in the most up-to-date laboratory, and ends with an interesting note on the application of a miscellany of the more unusual reagents.

The section of the book dealing with organic quantitative analyses is equally comprehensive and detailed, both macro- and micro-techniques being described for the determination of the main elements, specific groups, etc. Various alternative methods are presented; for example, the determination of carbon gravimetrically as carbon dioxide, by acid titration after absorption in baryta, or by determining the change in conductivity of the baryta solution. All the usual non-metallic and metallic elements are covered, as are also the distinctive groups, nitroso, azo, thiocarbonyl, methoxy, alkyl, etc.

The volume ends with an excellent section covering titrations in non-aqueous solvents, a subject which is still one of the most attractive fields for those interested in pure research. The theoretical approach is again clear; aprotic, protogenic, protophyllic and amphiprotic solvents are discussed in relation to the Brönsted–Lowry–Lewis theories. Visual fluorescent, photometric, conductimetric and potentiometric indicator systems are described for various non-aqueous titrimetric determinations, and typical reaction phenomena are given graphical representation.

There is no doubt whatsoever that an authoritative, detailed and scientifically propellent work of this nature will find its way on to the bookshelves of all institutions dealing with either the practice or teaching of analytical chemistry and will retain its status as a unique analytical vade-mecum for many years to come. D. T. Lewis

FREE RADICALS IN AROMATIC SUBSTITUTION

Homolytic Aromatic Substitution

By G. H. Williams. (International Series of Monographs on Organic Chemistry, Vol. 4.) Pp. vii+133. (London and New York: Pergamon Press, 1960.) 45*s*. net.

INTEREST in homolytic, as distinct from heterolytic, reactions dates from the recognition by Prof. D. H. Hey in 1934 that the nuclear phenylation reaction, discovered some ten years earlier by Gomberg and Bachmann, did not conform with current ideas of aromatic substitution in terms of reactions by electrophilic and nucleophilic reagents. He postulated that this reaction represented a new type of aromatic substitution involving electrically neutral free radicals. Further reactions displaying the same characteristics were soon discovered and were intensively studied. Homolytic substitution has since become a subject of considerable theoretical and practical interest.

In recent years, thanks to new and refined physical techniques, organic chemists have been able to accumulate reliable quantitative data on aromatic substitution processes of all types and this new knowledge has often necessitated a revision of theoretical concepts. The appearance of this monograph by Dr. Williams, a collaborator of Prof. Hey for many years, is timely, and it represents a valuable contribution towards a more comprehensive understanding of aromatic substitution generally.

The author subjects to critical scrutiny the various theoretical treatments, based on wave mechanics, which have been applied in attempts to rationalize the observed phenomena of aromatic substitution. Particular emphasis is placed on those aspects germane to the problems of orientation and reactivity in homolytic substitution. The limitations and deficiencies of these theoretical treatments are exposed. Thus, some unwarranted assumptions are made; for example, the failure to take cognizance of the intrinsic reactivity and polar characteristics of free radicals. Evidence, based on partial rate factors, is adduced to show that all homolytic substitution reactions exhibit some partial ionic character.

The reactions surveyed include homolytic arylation, both inter- and intra-molecular, alkylation, hydroxylation, acetoxylation, benzoyloxylation, amination

and amidation reactions. In the case of mercuration, the author concludes that the case for a homolytic mechanism has not yet been definitely established.

Not unnaturally, in this rapidly advancing field, there are controversial issues and divergence of views among the various schools, British, American and German. The author projects his own views, but still manages to present a balanced statement, commendably free of any polemical bias.

J. Idris Jones

THE CARTESIAN MEDITATIONS

Cartesian Meditations

An Introduction to Phenomenology. By Edmund Husserl. Translated by Dorion Cairns. Pp. xii + 157. (The Hague: Martinus Nijhoff, 1960.) 9.50 guilders; cloth bound 13.25 guilders.

ALTHOUGH it would be idle to deny that Edmund Husserl did otherwise than stand—in a certain restricted sense—upon the shoulders of Descartes, yet the break-through to phenomenology as a rigorous system of pre-suppositionless philosophy was an achievement of the master himself. In the end it was almost independent of Cartesian influences. Hence the paradox of the title *Cartesian Meditations* and all that flows from them. But it was one of those symbolic events of history which brought Husserl to the Sorbonne in February 1929 to deliver a couple of lectures, afterwards elaborated into the work now under review. He truly meditated in Cartesian terms, producing out of this exercise his transcendental phenomenology.

This is scarcely the place to discuss the content of these lectures—that has already been attempted in a review of the German script some years ago. The immediate aim must be limited to welcoming such a scholarly and meticulous English translation as is now available in the present book. Anyone fortunate enough to possess Vol. 2 of *Husserliana* can follow for himself (since the pagination is carefully co-ordinated throughout by marginal brackets) the exact course of this transliteration, and the subtle changes of mood inherent in Husserl's thinking. In fact, the reader has the advantage of a transcription from the text now called *Typescript C*, where, as in most cases, this comes nearer to the author's works which were published during his life-time. Thus, it is possible for English-speaking scholars not only to recapture what happened in Paris more than thirty years ago but also to study it in the setting of the lecturer's habitual mode of presentation as his own thoughts developed. Our debt to Dr. Dorion Cairns is great, and only a little less to the publishers for making this classic of epistemology more widely accessible.

To follow Husserl's 'concluding word' in the original is very difficult. Here, it becomes a little easier, and its message for science more capable of assimilation. It is something like this: our practical daily life is naïve, engulfed in a series of happenings which are just there (an element of brute fact), and continue quite impersonally. It should be noticed that this immersion includes the act of valuing, something which it has become customary to exclude from the natural sciences, but which modern thought seems to be bringing back in a species of subjectivism akin to that of Husserl. This tendency is important for the biological disciplines wherein objectivity is less coercive than in the domain of mathematics. Yet for Husserl, all science is naïve to some degree, metaphysics included. But metaphysics as such are allowable under certain conditions.

The meditations end most appropriately with the well-known Augustinian exhortation: "Do not wish to go out; go back into yourself. Truth dwells in the inner man".

F. I. G. Rawlins

BIOPOESIS

Aspects of the Origin of Life

(International Series of Monographs on Pure and Applied Biology. Division: Modern Trends in Physiological Sciences, Vol. 6.) Edited by M. Florkin. Pp. viii + 199 + 5 plates. (London and New York: Pergamon Press, 1960.) 30*s*. net.

MOST of the papers given in 1957 at the Moscow international symposium on "The Origins of Life" (see *Nature*, 180, 886; 1957) were precirculated; corrected texts, together with the discussion, were published in 1960. The symposium was planned along tolerant lines, and many of the papers dealt with a range of themes that, though interesting and important for an understanding of present-day manifestations of life, had no necessary connexion with its origins.

In all symposia of this type, viruses and nucleic acids loom large—apparently for the reasons that lead shopkeepers, whatever they may ostensibly be selling, to run a line in ball-point pens as well. Here we have a usefully pruned version of the symposium; the clutter of papers on ephemeral fashions in biochemistry (which move more sluggishly than women's fashions but equally irrationally) has gone and the relevant papers remain.

There are five papers on the probiotic environment. These show so much interesting conflict that it is clear that astronomical and geological evidence leaves ample latitude for speculation. Even the widely accepted view that the primitive atmosphere was anaerobic may be questioned because the amount of ferric iron and oxidized sulphur in sediments shows that more oxygen passed through the atmosphere at a very early stage than is present in it now. Four papers deal with processes that may be analogous to those that formed organic matter initially. As the complexity of the mixtures subjected to various agencies—ultra-violet light, electric discharges, heat, etc.—increases, by the inclusion of hydrogen sulphide, hydrogen cyanide and other probable primitive effluvia, a fascinating range of products, with affiliations to most groups of molecules now important in biochemistry, will be made. Few theories of biopoesis should be excluded on the grounds that the substrates could not have been available.

The remaining papers deal with the evolution of enzymes, the role of asymmetry, photochemistry, and other themes. They are well selected, and one's only regret is that modesty led the editor to exclude his own excellent paper on the frequency with which substances that are used for one purpose in primitive organisms find a different application as evolution proceeds. If this were more generally recognized it would discourage dogmatic attempts to extrapolate back from present-day biochemistry to the primitive state of affairs.

N. W. Pirie

Vacuum Technology Transactions

Proceedings of the Sixth National Symposium, also cumulative Author and Subject Indexes of 1954–59 Symposia. (American Vacuum Society Inc.) Under the Editorial Supervision of C. Robert Meissner. Pp. xvi + 335. (London and New York: Pergamon Press, 1960.) 120*s*. net.

THE symposium of the American Vacuum Society has become an annual event of international importance in the field of vacuum technology at which leaders in the subject from scientific and technological institutions, throughout the world, gather to read papers on their most recent researches. These papers are presented in detail in the *Vacuum Technology Transactions* which are usually published a few months after the symposium. The material covers almost every aspect of vacuum technology, from fundamental work of mainly academic interest to descriptions of the vacuum systems of the most recent particle accelerators and thermonuclear devices. The 1958 and 1959 volumes, however, show a noticeable increase in technological work directed towards the attainment of ultra-high vacuum in large machines. This is particularly true of the 1959 transactions, which include technical data associated with the design of the vacuum system for the Model *C Stellarator*, which will undoubtedly prove of great use to those facing similar problems. In addition to presenting the papers read at the conference, the 1959 *Vacuum Technology Transactions* contains a cumulative index of papers read at the previous symposia. The index is in chronological order, groups the papers in order of subject and is presented together with an author index arranged in alphabetical order, by year of presentation and page number. The combined index will be welcomed by those wishing to make a survey of recent research in a particular branch prior to embarking on work within the same field. The 1958 and 1959 *Transactions*, in keeping with the previous volumes, will be of considerable value to those who were not fortunate enough to be able to participate in the symposia and to those who wish to retain detailed information for future reference.

An Introduction to Electronic Theory of Organic Compounds

By H. L. Heys. Pp. 236. (London: George G. Harrap and Co., Ltd., 1960.) 16*s*. net.

THE writing of an elementary text-book is an art which is beset by difficulties. This is particularly true when the subject is the electronic theory of organic reactions. The evidence for electron shifts in molecules depends upon a wide variety of chemical and physical observations, and for an understanding of the significance of such measurements at least a thumbnail sketch of each method is desirable.

In developing his account of the subject the author has been aware of this need and he has been largely successful in his treatment of the problem. He has covered the main sections of the theory with an admirable conciseness and clarity, and the simpler aspects of any problem are clearly described without neglecting the minutiæ which may cause difficulties.

I am not, however, entirely in agreement with the author in devoting more than 20 pages to the Bohr and Sommerfeld treatments of the atomic orbitals, a discussion which seems to have no relevance to the remainder of the book. Moreover, some details included in the text do not seem to be in agreement with recent information. Thus, the idea that the two carbon-carbon bonds of ethylene have different energies is a theoretical concept rather than an experimental observation (p. 49). Also (p. 87) the value of 190 kcal./gm. atom $C_{(s)} \rightarrow C_{(g)}$ (^5P) has never been seriously supported.

The book is well produced with clear diagrams and a generous index. The only errors in production noted by the reviewer are 'C' for 'Cl' (last line of p. 78), a spacing error (line 10, p. 166) and the loss of a bond in tropolone (XXV, p. 110). These can be easily put right in the next edition.

R. I. Reed

The Veterinary Annual, 1960

Edited by W. A. Pool. Second year. Pp. xxiv + 359 + 32 plates. (Bristol: John Wright and Sons, Ltd., 1960.) 42*s*.

THE literature now being published on every aspect of veterinary science is so voluminous, and it records so many important advances in knowledge, that everyone who has to try to keep pace with it will welcome the appearance of a second volume in this authoritative series. For it gives us, under the able editorship of W. A. Pool, an epitome, selected by 35 specialists, of the important work done since the publication of the first volume of the series in 1959.

The field covered by veterinary research is nowadays very wide, and even a brief study of these pages will show how closely modern veterinary research is integrated with the work of other branches of science. Though the book is mainly for the veterinarian, it reflects the many facets of the study of comparative medicine and surgery, and it will for this reason interest all who are concerned with disease, whether they be medical men, especially perhaps those who are co-operating with the veterinarian, or chemists or others who provide us with so wide an array of drugs and other compounds used in the battle with disease. The nomenclature of these compounds is, as the editor puts it, 'harassing' to many who have to try to understand their composition and uses, and welcome features of this book are the appendixes to the articles on drug therapy and on insecticides and acaricides, which give, together with the chemical names, the trade or proprietary names used for them in different countries.

For those who are interested more in the general aspects of progress of veterinary work there are special articles on veterinary medicine in the United States, the Netherlands and France, written by experts in these countries, an article on veterinary medicine in the British Colonial Territories, two others on the challenge of *Brucella* and on the poultry industry and—graceful reminder of the interests of youth nowadays—a well-written and practical article on "The Child, the Pony and the Veterinary Surgeon". The Secretary of the Royal College of Surgeons contributes an article on legal matters affecting the veterinary profession, and there are chapters on new drugs and appliances and a list of new English veterinary books and new editions.

This book, like its predecessor, should be in every library concerned with the study and control of disease, and it is to be hoped that nothing will prevent the appearance of future volumes in the series.

G. Lapage

GENERATION OF ELECTRICITY WITHOUT THE USE OF ROTATING MACHINERY

By Dr. K. H. SPRING
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A COURSE of lectures on direct processes for the generation of electricity has recently been given at University College, London, under the above title. An introductory survey was given by me. The main object of the lectures was to give an idea of the scientific principles and possibilities, rather than to describe the engineering of devices.

The principles of many of the direct processes have been known for a great many years, but the recent rise in interest is probably attributable to several factors. It seems likely that advances in efficiency above about 40 per cent of the heat engines (steam or Diesel) used for large-scale power generation will be achieved only with extreme difficulty. There is a possibility that some of the new processes may ultimately permit a major advance in generation efficiency to be made, and also lead to a lowering of capital costs. New requirements for electric power for military and other specialized uses, such as operation in remote sites or in space-vehicles, have created a demand for compact, simple, and in some cases silent, devices in which the relatively low conversion efficiency so far attained is not of great economic consequence. A further factor is that in recent years advances in technology and physical understanding have enabled new classes of materials with interesting electrical properties to be developed.

The classical effects of an electric current are magnetic, chemical and thermal, and, in the reverse process of generation, it is only the first of these—moving a metallic conductor in a magnetic field—that has been used at all widely. A number of generation processes can now be listed, some of them based on direct chemical and thermal effects. The first three (or possibly four) of these may ultimately be developed sufficiently to supplant or supplement present methods of large-scale generation, but the others are likely to be of specialized application only.

(1) The Fuel Cell

This is an electrochemical device in which the processes occurring are almost the converse of those in electrolysis. Fuel (usually in the form of a gas) is fed to one electrode, and an oxidant to the other. The electrodes are separated by an ion-exchange membrane or an electrolyte which ensures that only ions can move from one to the other, balance being maintained by the flow of electrons, constituting the current, in the external circuit. Because the free chemical energy is released by a directed flow of ions, and not by degradation into a random thermal motion of molecules, the fuel cell acts isothermally and escapes the Carnot limitation inherent in all heat engines. Consequently, the apparent thermodynamic efficiency may be very high—more than 90 per cent. However, as soon as any current is drawn from the cell there are ohmic and polarization losses which lower the open-circuit voltage, just as they do in a primary battery. The fuel cell is usually operated at a current density that gives an efficiency in the region of 60–70 per cent.

Apart from various exotic fuels and oxidants that may be used for special purposes, hydrogen and oxygen (or air) are most easily ionized and combined at temperatures around 20–200° C., and the work of Bacon at Cambridge, and of Shell and other companies, is well known. For central power generation, hydrogen even if impure is too expensive a fuel, and for economic parity with conventional methods it would be necessary to use the cheapest possible gas based on total gasification of coal, or on re-formation of oil products. The use of such a gas requires further development of a high-temperature fuel cell, using a molten salt electrolyte which is stable to carbon monoxide and dioxide, rather than the simple aqueous alkaline electrolyte of the Bacon cell. Research on such cells is being actively pursued in many countries.

(2) Magnetohydrodynamic (MHD) Generation

This is the name which is now employed to denote direct extraction of electrical energy from a fast-moving conducting fluid passing through a magnetic field. The principle is similar to that of an electromagnetic flowmeter which measures the voltage developed between the ends of a conductor moving in a magnetic field. A gas which has been raised to a temperature high enough for some thermal ionization to take place, say 2,500° K., may be used as the working fluid, the conductivity being raised still further by 'seeding' with a low work-function material such as potassium. The upper temperature is limited by the combustion process itself, and also by problems of combustion chamber and duct materials. At the highest temperatures envisaged only a fraction—less than 1 per cent—of the molecules are ionized. The possibility of generating power at appreciable efficiencies, therefore, depends on the transfer of kinetic energy from the uncharged particles to the ions and electrons which alone interact directly with the magnetic field, and thence by some mechanism to an external circuit. Very high gas velocities, of the order of Mach 1, are also needed. Supersonic working would allow higher efficiencies to be attained, but would pose difficult aerodynamic problems.

Because of their high mobility, most of the current in the plasma is mediated by electrons rather than ions and in a continuously acting device electrodes must be provided to maintain charge equality. It is difficult to conceive of electrodes that will emit for long periods in an atmosphere charged with combustion products, and a system of pulsed or cyclic working which will permit inductive coupling may be necessary. The use of electrodes may be feasible in a clean working fluid which is heated indirectly,

for example, by a nuclear reactor. Further research may suggest ways in which ionization can be obtained at lower temperatures by non-thermal means. This would be helpful from the point of view of materials, but would be less attractive thermodynamically.

(3) Thermionic Generation

This implies the 'boiling-off' of electrons from a heated cathode surface to a nearby, cool, anode. (A very small current may be obtained from a diode valve with the heater emitting, but with zero anode voltage.) The separation between the electrodes must be extremely small in a vacuum diode (about 0·01 mm.) to minimize the effects of space charge in limiting the current. Such a small separation may not be practicable on a large scale, and attention has therefore been devoted to alternative methods. Most of these are based on the injection of ions into the inter-electrode space. Cæsium in contact with a hot cathode surface readily ionizes, and such cæsium diodes are sometimes described as plasma thermocouples, by analogy with the more usual solid-state thermocouples.

A thermionic generator is a heat engine, and its efficiency is limited to that of a Carnot cycle operating between the temperatures of the cathode and anode. The former should therefore be as high as possible, consistent with the desired life of the diode. In practice, the thermal radiation loss from the cathode to the anode is a factor seriously limiting efficiency. The use of crossed electric and magnetic fields which guide the electrons from one electrode to the other may reduce space-charge effects and also permit geometries which minimize radiation losses. The voltage developed by a diode depends on the difference in work-function between the cathode and anode. One advantage claimed for cæsium injection is that it reduces the anode work function. Development of maximum power depends on proper matching of the load.

(4) Thermoelectricity

Both the theory and practical applications of thermoelectricity have made tremendous strides in the past few years—due in large measure to Joffe. The usefulness of a thermoelectric material depends on three factors—the thermoelectric (Peltier) coefficient α, and the electrical conductivity σ, which should be as large as possible; and the thermal conductivity K, which should be as small as possible. The 'figure of merit' $Z = \alpha^2\sigma/K$. For metals, in which the electrons are nearly free, α is low—only a few μV./deg. C., but in some semiconductors α can be much higher. The three factors contributing to Z are not independent. To obtain the highest value of Z in a semiconductor, the material is prepared, either p- or n-type, by 'doping' to optimize α to a value in the region 200 μV./deg. C. It is found that the highest value of Z which can be achieved depends on the temperature at which the material operates, and ZT gives a truer impression of usefulness. (T is the absolute temperature.)

The value of σ/K is nearly fixed, being determined by the Wiedemann–Franz ratio in metals. In semiconductors the crystal lattice contributes to the thermal and electrical conductivities; it seems likely that it will not be possible to reduce the lattice (or 'phonon') contribution to less than that of the electrons, which would limit ZT to 4, corresponding to 37 per cent of Carnot efficiency for a given temperature-range. In the most advanced materials now available, it is several times higher, and the best values of ZT are about 1 for both p- and n-type materials, corresponding to about 15 per cent of Carnot.

Moderate voltages may be generated by arranging alternate p- and n-type materials which are thermally in parallel, but electrically in series.

(5) Thermomagnetic Generation

If two coils, of which one (the primary) is carrying a current, are wrapped around a core of ferromagnetic material, the flux linkage with the secondary will change if the permeability of the core changes. Thus, an alternating voltage may be induced in the secondary if the core is temperature-cycled around the Curie point. In a sense this may be regarded as a form of parametric amplification of the signal in the primary, the required energy being provided thermally. Gadolinium, with a Curie point of 27° C., has sometimes been suggested as a useful, if expensive, material to use where a source of heat a few degrees above normal ambient temperatures is available. There has been some controversy over the efficiency of the generator. It appears that quite high Carnot efficiencies can be obtained in the immediate neighbourhood of the Curie point, but a range of, say, 20° C. between source and sink may correspond to only 3° on the specimen. This, coupled with the fact that, to cover any large temperature-range, cascading is needed, makes thermomagnetic generation in practice compare very unfavourably with thermoelectric.

(6) Ferroelectric Generation

It is possible to generate voltages of the order of 1,000 by making use of the variation with temperature of the permittivity of a ferroelectric material, such as barium titanate. The material is made the dielectric of a capacitor, which is charged at its Curie temperature at which its permittivity is maximal, through a small battery via a holding diode. If the temperature of the dielectric is changed, the capacitance falls, and the voltage rises, since the diode prevents loss of charge. The permittivity of a dielectric under electric stress is nearly constant at all temperatures below the Curie point, so it is necessary to cycle it from the Curie point to a temperature above it. Again, this method can be regarded as a form of parametric amplification of the input signal supplied by the battery. Circuits have been developed so that, at any instant, a number of capacitors are in different phases of the thermal cycle, and only a small initial charging is needed: this forms a convenient method of generating high voltages for use in space vehicles.

(7) Photovoltaic Converters (Solar Cells)

The earliest type of photovoltaic generator is represented by the selenium photocell, which had a conversion efficiency of about 0·2 per cent when exposed to sunlight. Its modern counterpart, of silicon, has been developed largely as a result of research on transistors. Its action depends on the penetration of radiation to a p–n junction, so the cell is in the form of a disk of n-type material, on the top of which is diffused an extremely thin p layer.

The photovoltaic cell somewhat resembles the thermocouple in embodying p–n junctions; but the physical mode of operation is rather different. The former depends on photons penetrating to the junction with sufficient energy to raise electrons from the valence band to the conduction band. Since the forbidden energy gap (activation energy) of silicon is 1·1 V., the radiation must be shorter in wavelength than about 1μ. However, because some electrons are attached to impurity atoms, and are therefore more nearly free, there is some response at wave-lengths beyond the quantum cut-off. The efficiency of present solar cells is about 15 per cent to sunlight, so that 150 W./m.² may be generated at sea-level in clear weather. As the present cost is about £10,000/m.², only very specialized applications can be considered. Cells based on more advanced materials such as gallium arsenide and cadmium telluride may possibly attain efficiencies of about 25 per cent.

(8) Piezoelectric Converters

When magnetic or electric fields are applied to certain materials there are dimensional changes, and the converse is also true. Thus, when pressure or shear forces are applied to some types of crystal (for example, quartz) a potential difference is created, and this is the principle of operation of some types of gramophone pick-up. Recently, synthetic materials have been developed suitable for the generation of very high voltages and one of the best now available is 'PZT', a solid-solution ceramic of lead titanate–zirconium titanate. Its piezoelectric coefficient is such that a voltage gradient of about 10 kV./in. is produced for a pressure of 1 ton/in.². The maximum pressure that can be withstood for repeated rapid stressing is in the range 1–5 ton/in.² so that voltages of 20 kV., suitable for petrol engine ignition systems, can be produced from quite small pieces of material by direct pressure and without the intermediary of coils or breakers. Piezoelectric generation is a method for converting mechanical to electrical energy, and therefore is not in competition with other methods for direct generation from heat or fuel. Nevertheless, it is likely to revolutionize the design of electric ignition systems on vehicles.

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MECHANISMS OF EXPRESSION OF GENETIC INFORMATION

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DURING several years past, the overall pattern of protein synthesis has become fairly well established. This pattern indicates that the genetic information inherent in the chemical structure of deoxyribonucleic acid (DNA) is in some way incorporated into the structure of ribonucleic acid (RNA), which then possesses the capability, in the presence of suitable precursors, of guiding the polymerization of specific sequences of amino-acids into protein[1]. We have considered mechanisms by which the DNA may be able to carry out such communication mediated by RNA with the rest of the cell.

It is well documented that a molecule of DNA is composed of two strands, one of which is the reciprocal of the other in a base-pairing sense[2]. For this reason, the information in a single DNA molecule is actually repeated, once in each strand. However, it may quite well be that the cell is only able to 'recognize' one of these information strands, at least so far as the polymerization of an RNA molecule is concerned. This would be the net result of either of the two following mechanisms: (1) RNA synthesis is directed by the two-stranded DNA duplex, but can proceed in one direction only; or, (2) RNA synthesis is directed by a single DNA strand, but only one of the strands is capable of serving as a template. This type of restrictive mechanism might result from the same sort of chemical restraints which give the enzyme polynucleotide phosphorylase its unusual specificity with respect to the polymerization of cytidylic residues as compared to guanilic residues[3].

A second alternative, which is functionally equivalent to the above, is to suggest that both DNA strands are capable of coding RNA, but that one of the two RNA strands produced cannot code protein, either because it is left in a form vulnerable to cellular ribonucleases, or because it becomes stabilized in a non-functional ribonucleoprotein complex. This alternative can also be applied to the case in which both RNA strands are capable of coding protein, but with the additional condition that one of the product proteins be regarded as non-functional or non-resistant to proteolysis. This suggestion, which states that one of the two possible RNA strands derived from a DNA molecule cannot make a 'good' protein, is quite logical when one considers that a point mutation in the original DNA duplex will necessarily change both the RNA strands and consequently both their possible product proteins. To expect that evolutionary selection would preserve both proteins in a functional form is not reasonable, in view of current knowledge on the manner in which amino-acid sequence directs protein structure.

The last and most attractive alternative for the communication of information contained in DNA is to postulate that each strand of the DNA duplex directs the synthesis of an RNA molecule complementary to itself. The difference between this alternative and that already discussed arises when we consider what the cellular environment can do with these two reciprocal RNA molecules. We suggest that one of these molecules, on separation from its DNA parent, encounters a specific protein which has both a tendency to aggregate with molecules like itself and a high affinity for certain regions in the

RNA. This affinity may be explained by the ability of this protein to recognize a certain specific sequence of bases repeated at intervals along the RNA molecule. However, it is apparent that mutations affecting this sequence would not destroy its recognizability so long as the general character of these sections is preserved. Thus, evolution might well have modified these repeating regions into sections of similar character the function of which would not be dependent on an absolute sequence. In any event, the RNA-protein complex so formed 'crystallizes' to form microsomes or ribosomes—structures which permit the exposure of the coding bases functional in the sequential ordering of specific amino-acids. This 'crystallization' of the ribosomal protein with its RNA may well be the basis of the mechanisms for the separation of RNA from its DNA parent. (If a similar specific affinity of an aggregating protein occurred for a strand of DNA, this could provide a mechanism by which the small, single-stranded DNA viruses select one strand for building into the nucleoprotein and exclude the other.)

The second RNA molecule, possessing a base sequence reciprocal to that of the molecule already discussed, will not have this affinity for the ribosomal structural protein. However, it could possess an affinity for a second type of protein, which may well be the protein which binds soluble RNA (*S*-RNA) and which is characterized by having the activity of the amino-acid activating and transfer enzymes. However, due to the lack of interaction of this type of protein with itself, this ribonucleoprotein (RNP) is not compact and resistant to cellular hydrolytic enzymes. It is therefore cleaved at all those points where the protein attachment does not protect it, and thus gives rise to a large number of RNP molecules. It is postulated that this family of small RNP molecules can now be acted upon by enzymes which have evolved in the cytoplasm. Certain of these enzymes will trim away parts of the ends of the bound RNA, others will link these modified RNP molecules with nucleotides such as 5-ribouridilic acid, and others will add nucleotides such as cytidylcytidyladenylate to the 3'-end and to the 5'-end nucleotides such as guanidylate, giving rise, finally, to a molecule which has the properties of the amino-acid activating enzyme – *S*-RNA complex, and which further contains within its nucleotide structure those base sequences which are reciprocal to certain regions of the ribosomal RNA. Thus, this *S*-RNA is automatically equipped with nucleotide sequences capable of pairing both with the enzyme activating the amino-acid and with that section of the ribosomal RNA corresponding to the reciprocal sequence of bases which specifies the particular amino-acid.

This hypothesis provides a clear and internally consistent mechanism for the efficient utilization of both strands of information of the DNA, and, further, a mechanism for the synthesis of both soluble and ribosomal RNA. It predicts phenomena which should be usable in testing the hypothesis; namely, the synthesis of *S*-RNA should not occur without the dependent synthesis of ribosomal RNA; and, assuming equivalent efficiency or 'turnover numbers' of the two complementary DNA strands (this RNA could be modified in quantity but not in quality by the efficiency of the appropriate protein in stripping the RNA from its DNA parent), the induction of a specific family of RNA, such as occurs upon the virus infection of a bacterial cell, should lead to the production of ribosomal and *S*-RNA, the next neighbour patterns of which when tested with isotopically labelled phosphate should follow the same reciprocal rules that have been found for double-stranded DNA[4]. This hypothesis may also offer reasons for various phenomena which have not as yet been satisfactorily explained. For example, it is known that there exist organisms which do not seem to have any of their DNA molecules in common[5], but which still appear to be able to synthesize similar, if not identical, proteins. Using our postulated mechanism of information transfer, this would be explained by assuming that those regions of the DNA responsible for the sections of RNA concerned with the recognition of ribosomal structural protein could differ markedly between two organisms, and thus, even though their equivalent DNA molecules carried the same encoded message, the DNA composition could vary within wide limits. Thus, the same 'code' between nucleic acid and protein can be used in all organisms, without demanding that their DNA molecules be identical. A second problem which may be partially answered is that of the development and intracellular recognition of DNA molecules derived from individual chromosomes. We suggest that each chromosome has its own general repetitive base sequence; this sequence again being that responsible for the sections of its RNA which have the function of recognizing the ribosomal protein. This would provide a definite distinction between DNA molecules produced in differing chromosomes; a distinction which may be used by the cell to retain DNA molecules within their proper chromosomes through an interaction with the chromosomal protein. This postulate could be tested by the banding, in a high-resolution density gradient[6], of the DNA isolated from organisms with a small number of chromosomes, and observing whether the number of bands is correlated with the number of chromosomes or linkage groups.

We possess little information on the nature of the precursors of the elaborate genetic forms we see to-day—too little to permit any detailed speculation on the early stages of evolution. Nevertheless, the reader may enjoy, as we have, speculating on the way in which a short primitive polynucleotide double strand, one-half with an affinity for peptide which aggregates readily, and the other strand with an affinity for a poorly specific peptide catalyst of polymerization reactions, could provide a base upon which mutation could play until more elaborate forms of life resulted.

After we submitted this manuscript, Prof. G. H. Echols kindly brought to our attention an earlier proposal of one of the above mechanisms for producing template RNA and amino-acid-transferring RNA[7].

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THE 2-METRE UNIVERSAL REFLECTING TELESCOPE OF THE GERMAN ACADEMY OF SCIENCE, BERLIN

By Dr. RUDOLF JOBST
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ON October 19, the Government of the German Democratic Republic placed at the disposal of the German Academy of Science a 2-m. universal reflecting telescope, which was designed and built by VEB Carl Zeiss of Jena, and inaugurated on that day in the newly erected Karl Schwarzschild Observatory in Tautenburg, near Jena.

The 2-m. universal reflecting telescope is outstanding as a type and represents the first and largest of its kind in the world. Embracing four different optical arrangements, the new telescope provides for the entire field of present-day astronomical and astrophysical work and the problems which are likely to arise in the future. The optical systems are interchangeable and conveniently adaptable to certain specific problems of observation and, in each instance, afford the same high performance as would a correspondingly large telescope individually built for the respective type of observation.

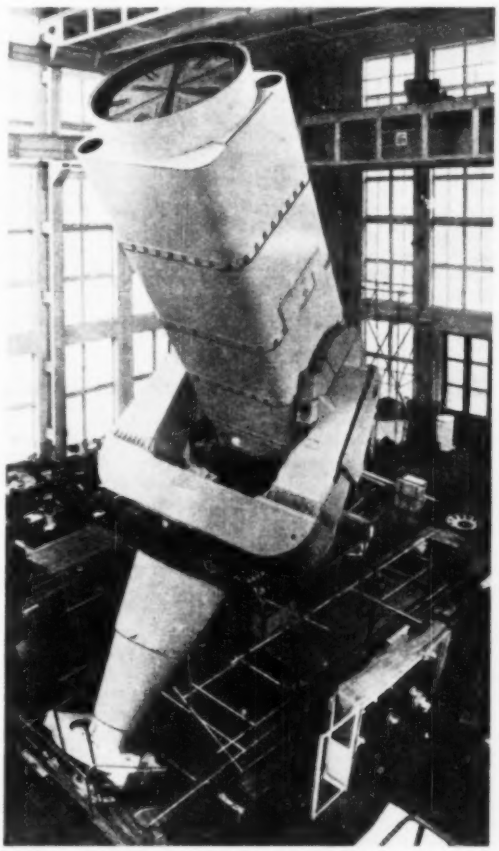

Fig. 1. The 2-m. universal reflecting telescope in the assembling department for astronomical telescopes of VEB Carl Zeiss, Jena

Thus, for investigation of extra-galactic objects, such as the structure of the Milky Way, as well as for the compilation of routine astronomical observations, the new telescope embodies the Schmidt system with the 2-m. spherical main mirror and 1·34-m. correction plate, with a 4-m. focal length and an aperture ratio of 1 : 3. In this form the Schmidt system of the telescope represents the largest in the world. It permits photographs 24 cm. × 24 cm. to be taken of portions of the stellar regions about 11 square degrees in size.

For the individual examination of cosmic gas clouds, distant spiral nebulæ and other faint objects in the universe, the quasi-Newtonian system with its high light-gathering power is employed, for which the full aperture of the reflector is used. In this case a small lens-correction system is interposed immediately in front of the image plane in order to compensate for the errors which a spherical concave mirror produces when used in this way.

With the quasi-Cassegrain system of the new reflector telescope, spectrographic investigations of fixed stars may be carried out down to the faintest luminosities, predominantly by photo-electric photometry and spectrography. Owing to the effective 20-m. focal length of this system, the examination of single stars is possible even in regions of greatest stellar abundance. In the quasi-Cassegrain system a super-hyperbolically deformed convex mirror 400 mm. in diameter is used with the 2-m. concave mirror.

The quasi-coudé system, with the same optical arrangement, but with another convex mirror of greater light-gathering power, and with a 92-m. effective focal length, permits, with the stationary focal image and with spectrographs for the highest dispersions, the study of the fine structure of the spectral lines of stars. Through one of the two bearing journals of the telescope tube, and through the large horseshoe mount, the optical path is conveyed via other plane deflecting mirrors down to the lower end of the main axis of rotation, which is aligned parallel to the Earth and is diverted into the spectrographs located in well-isolated rooms in which constant temperature and humidity are maintained. Astronomical and atomic physicists are using this equipment for research in which both are interested. Indeed, the cosmos affords them research facilities far beyond those available in experimental laboratory activities.

Mechanically, the telescope consists of a square-sectioned tube of about 10 m. length on a horseshoe mounting (Fig. 1). The moving parts of the telescope weigh 65,000 kgm., and therefore special arrangements, including a hydraulic bearing, are used for

following the movement of the stars with the necessary accuracy. The telescope floats on an oil film 0·05 mm. thick and is moved with the required accuracy by means of a precision worm-gear 2,160 m. in diameter, the teeth of which deviate from the mean theoretical interspace by less than 0·5 sec. of arc.

The movement of the 26,000 kgm. tube about the declination axis, as also about the polar axis, is via a 'Selsyn' transmitter conveyed to a central control desk and several side desks, whence the instrument may be set entirely electrically for the astronomical co-ordinates of celestial bodies. By means of a number of compensation devices the adjustments and seatings of the optical parts of the telescope in different positions are preserved at maximum accuracy under varying temperature conditions.

The 2-m. main reflecting mirror, weighing 2,370 kgm., as well as the correction plate of thickness 38 mm., and the different auxiliary mirrors, were cast by the VEB Jenaer Glaswerk Schott and Gen., which also attended to part of the preparatory work. What must be looked upon as outstanding performances in the province of astronomical optics are the correction plate, made of glass transparent to ultra-violet radiation and the two Cassegrain and coudé-counter mirrors, the mirror surfaces of which depart from a sphere by no more than 0·05 mm.

The Zeiss spectrographs, which are still in the manufacturing stage, will be equipped with diffraction gratings capable of producing stellar spectra up to a maximum length of 1,500 mm. At the inauguration of the Tautenburg Observatory, the Soviet Academy of Science presented to the Observatory one of these diffraction gratings, in addition to those produced by VEB Carl Zeiss.

The 2-m. universal reflecting telescope and all its appurtenances are housed in an observatory dome 20 m. in diameter and of a total weight of 175 tons, built by VEB Carl Zeiss. The building is heat-insulated, thus effectively preserving the night-temperature within the dome in day-time, despite solar radiation and other heat effects to which the dome may be exposed. Adverse fluctuations of temperature are avoided in this way, or are at least considerably diminished.

While work with this new 2-m. universal reflector telescope has been successfully begun at the Tautenburg Observatory, three more reflector telescopes of the same dimensions are in the process of construction in the Jena Zeiss works at Jena, two for the U.S.S.R. and one for Czechoslovakia. These instruments will benefit by the experience which had been collected during the development, construction and testing of the Tautenburg telescope.

A CHEMICAL BASIS FOR THE CLASSIFICATION OF ANIMAL VIRUSES

By Dr. P. D. COOPER

Director, Virus Culture Laboratory, Medical Research Council Laboratories, Carshalton, Surrey

BESIDES satisfying the intellectually tidy, an efficient taxonomy is useful and necessary because it emphasizes resemblances which make worthwhile generalizations apparent, and makes minor differences easier to understand. The possible objection that viruses may not form a single natural taxonomic group need not inhibit attempts to define one. Several systems have in fact been proposed to classify animal viruses[1,2] but have not proved very suitable, and virologists have generally agreed on the need for more data.

However, the earlier systems were based mainly on habitat at the level of the intact animal (that is, host-range, type of tissue usually affected, host-response and type of lesion produced, or vectors), and this now seems a major fault, since many objections can be levelled at such a primary subdivision[3]. For example, 'obviously' different viruses (foot-and-mouth disease and cow-pox viruses) can produce somewhat similar lesions, albeit at opposite extremities, of the same animal. Host-animal reactions may vary with the one virus (for example, chickenpox and herpes zoster[4]), and are a very complex expression of growth at the cellular level. Viruses can often be adapted to unusual hosts without much difficulty. Grouping by known hosts seems an arbitrary procedure, since many hosts may be unknown and thus only a few of the creatures potentially infected are selected; again 'obviously' different viruses (for example, myxoma and yellow fever viruses) can both depend on a similar vector (mosquitoes). Tissue tropism can be genetically very unstable: poliovirus can mutate in one step from neurotropic-plus-viscerotropic, to purely viscerotropic, and back again[5], and host-range variants of encephalomyocarditis virus are easy to obtain by a single growth cycle[6]. Cultured cells normally resistant to intact poliovirus can nevertheless support maturation of virus if infected with ribonucleic acid extracts of infected cells[7]. Adenoviruses have been found in stools[8], and might therefore legitimately be called 'enteroviruses', along with poliovirus.

It is therefore very doubtful whether habitat, as defined above, is at all suitable as a primary criterion for classification of animal viruses, although, as discussed below, it may be useful at another level of emphasis.

All systems of biological classification depend on mutationally stable criteria; indeed, the closeness of all biological relationships might in time be judged by the number of mutations which separate them, although this reasoning is easier to accept for the present when applied to sub-species and to interrelated micro-organisms. The difficulty with viruses is that they are genetically unstable when judged by human time-scales, appearing in a state of rapid evolution, so that a classification denoting species and genera is difficult to apply[9]; attempts at a quantitative appraisal of the genetic differences without emphasizing one criterion more than another

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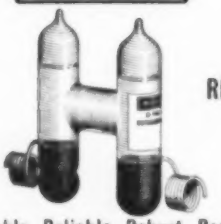

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are likely at present to run into difficulties for lack of data.

What is needed to provide a lasting system for the classification of viruses is to obtain some primary and secondary sub-divisions which are not too arbitrary and which ought to be genetically quite stable. It is the purpose of this article to emphasize the need for genetic stability, and to point out the utility of a formal system based on lines of thought already familiar to many virologists, the high genetic stability of which, however, is possibly not fully appreciated as a classification criterion.

Nucleic Acid as Primary Criterion

The basis of the system proposed is the chemical structure of the 'virion'[10], that is, the largest free-existing infective unit which can be defined as a single virus particle (usually the infective unit occurring naturally in largest numbers). It is primarily concerned with the type of nucleic acid contained, since this is the one component always essential for the production of infective virus; the chance of interconversion of deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) by simple mutation is vanishingly small, if not impossible, so that this criterion should be quite stable. Another advantage is that this criterion must apply to all viruses, yet in an exclusive way. Present genetic concepts demand that a virus must contain either RNA or DNA or conceivably both; if the psittacosis group is excluded, the existence of both in any virus is doubtful, but the possible presence of RNA in a DNA-containing virus (for example, the pox group) need not affect the classification proposed. The only ambiguity may arise in the hypothetical case where the same total of information can be carried by either DNA or RNA in a single form acceptable to a host cell, thus giving two phases for the same virus. Fortunately consideration of this objection can be deferred until it can be raised experimentally. It is submitted that the terms 'RNA virus' and 'DNA virus' are terminologically improper; to avoid the clumsy phrases 'ribonucleic acid-containing virus' and 'deoxyribonucleic acid-containing virus', the terms 'ribovirus' and 'deoxyvirus' are suggested.

Essential Lipid as Secondary Criterion

The secondary sub-division uses the criterion of ether sensitivity, suggested for classification purposes by Andrewes and Horstmann[11]. Destruction of infectivity by lipid solvents (which appears to be correlated with sensitivity to low concentrations of detergents[12,13], and in the case of Newcastle disease virus[14] with sensitivity to lipase) presumably reflects the presence of fatty components essential for infectivity. Those viruses insensitive to ether and detergents either do not contain lipid (for example, poliovirus[15]), or their lipid content is tightly bound or not essential (for example, vaccinia[16]). The genetic stability of this criterion is less certain than that of difference in nucleic acid content, but two facts suggest that it is non-trivial and that it should be fairly stable (that is, not readily lost by non-lethal mutation): (*a*) the ether-sensitive particle of influenza virus breaks down completely when the lipid is removed[17]; (*b*) among riboviruses, the sensitivity to ether correlates with maturation at the cell wall[18], suggesting a widespread mechanism involving lipid materials without which the viruses cannot become infective.

In practice and excepting the pox group, viruses appear either to be quite stable to ether, or to be very sensitive (provided that they are tested in an accessible state and not protected within a mass of tissue), making it a fairly easy criterion to apply. Those ether-resistant viruses so far examined (for example, poliovirus[19], adenovirus[20], polyoma virus[21]) have a strong and regular lattice-like (clathrate) substructure, whereas the ether-sensitive viruses are less rigid[22], tending also to flatten more in electron microscopy. Accordingly, the terms 'clathrovirus' and 'lipovirus' are suggested for the ether-resistants and ether-sensitives respectively, to apply to the infective form only (as some lipoviruses, for example, herpes virus[23], may contain clathrate substructures).

Consideration of Major Groups

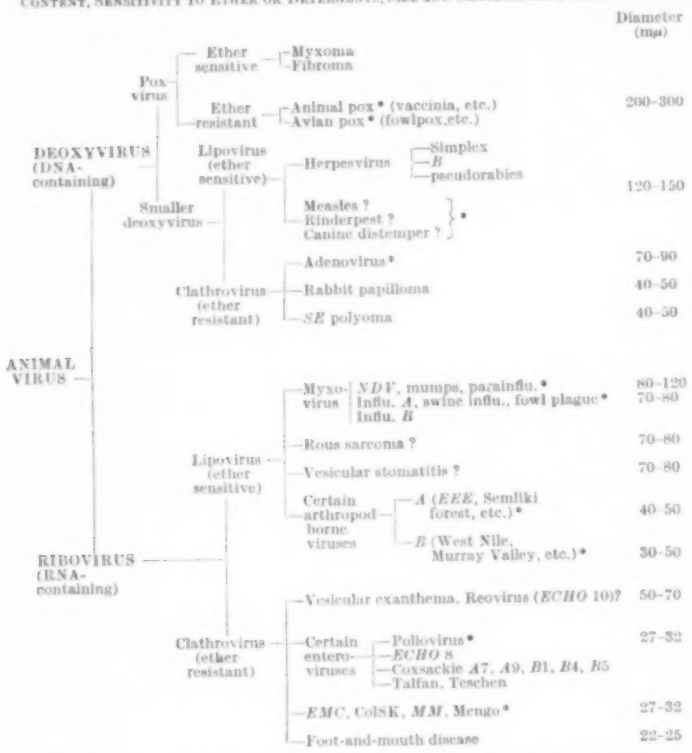
When these two types of separation are made, and the viruses the positions of which are known then arranged in each of the four major subdivisions in order of size, a considerable degree of order results (Table 1), and the viruses are brought together in groups which are often immunologically related. Four principal chemical relationships are therefore used: nucleic acid type, content of essential lipid, size and immunological character; it will be noted that 'chemical' is here used in its widest sense, and that among entities of the size of viruses there is little difference between chemical content and fine morphology. There will, of course, be gaps, many known viruses cannot yet be placed, and the placing of some viruses (marked with a query) is based on rather slender data, but the position of most is reasonably well based for at least one member of a serological group.

It will be noted that the pox-viruses are treated as a special case, and this is for two reasons. First, separation into ether-sensitive and ether-resistant has the effect of separating myxoma/fibroma from the vaccinia and avian-pox groups[11], and, although there are some reservations about their relationships[24], recent work[25,26] shows their closeness by reactivation and serological data. Secondly, vaccinia nucleic acid clearly replicates in the cytoplasm[27], whereas the nucleic acid of all other viruses adequately studied (herpes virus[28], adenovirus[29], encephalomyocarditis[30] and fowl plague[31]) replicates in the nucleus. The pox viruses therefore seem metabolically more autonomous than smaller viruses, and there is a strong case for regarding them as a distinct group intermediate between the smaller viruses and the ornithosis group.

Because of its inherent genetic stability the nucleic acid type is preferred as a primary criterion, and, because of its observed genetic instability in some cases, immunological character is set last, but the relative stability of the other characters is not predictable. The viruses also come together in groups of similar habitat, and it may be that this admittedly useful grouping, while unsuitable as a primary criterion, could be applied as a tertiary one.

Deoxyviruses are generally larger than riboviruses although overlap does occur. Lipo-riboviruses tend to be larger than clathro-riboviruses. Thus some generalizations can be made from this system, since the primary and secondary criteria also separate other properties, and this should help the understanding of the structure and growth mechanisms of new viruses if these criteria can be applied.

Table 1. A Classification Scheme for Animal Viruses Based on Nucleic Acid Content, Sensitivity to Ether or Detergents, Size and Serological Relationships



• Serological group. Data on vesicular exanthema from Shaffer and McClain (personal communication)

Conversely, other properties can help classification when the criteria cannot yet be applied. For example, the large size of measles virus[32], the formation of large intranuclear inclusions and its intracellular mode of growth all suggest that it is a deoxyvirus. Rous sarcoma[11] and vesicular stomatitis viruses are both lipoviruses; there is evidence, not firmly based, that both are riboviruses, and their continuous mode of release[33,34] strongly supports this idea.

At the moment there appears little evidence to contra-indicate the classification of Table 1, although other arrangements are possible; for example, one may regard size as more important than ether sensitivity and promote it to secondary criterion, but the large differences in size among the smaller viruses makes deciding the border-line arbitrary and inconvenient. From a practical point of view, determination of reaction to ether is much easier than determination of size. Good evidence against the proposals would be the finding of strong serological relationships between the main groups differentiated in Table 1.

Correlations with Growth Properties

The separation into four main groups accords well with growth properties, where these are known. In fundamental replication mechanism (that of the nucleic acid) one must expect deoxyviruses to resemble one another more than riboviruses, and vice versa, although a possible exception to this is the small single-stranded DNA-containing phage[35], the replication of which may resemble a ribovirus. The deoxyviruses (vaccinia, herpes and adenovirus as examples) are slow to mature and to be released, and form marked inclusion bodies, but the riboviruses mature much faster and do not form marked inclusions.

The lipo-riboviruses (for example, vesicular stomatitis, influenza, Western equine encephalomyelitis, fowl plague) appear to be matured at the cell wall[18], whereas the clathro-riboviruses mature internally (for example, poliovirus, encephalomyocarditis, foot-and-mouth disease, vesicular exanthema), probably in the cytoplasm. This differentiation does not apply to the deoxyviruses, which all mature internally, but in this case the core of a lipovirus (herpes), although being formed in the nucleus, receives a final coat (and therefore is matured ?) on entering the cytoplasm[36], whereas a clathrovirus (adenovirus) appears to be completed in the nucleus[29].

It is interesting that viruses capable of causing proliferative lesions, even if finally necrotic, occur in all groups except the clathro-riboviruses; haemagglutinins of one sort or another are also found in all groups except the lipo-deoxyviruses, indicating that neither of these phenomena is related to a particular virus type, and is therefore *per se* of small value for classification purposes.

Means of including more Viruses

It may be felt that it is impractical to determine the nucleic acid present in a large number of viruses in order to classify them, even if one selects only a single member from each serological group. However, this information is urgently necessary, since it is an essential preliminary to understanding the most fundamental part of their growth processes, representing probably the most important single datum, and providing a most useful guide to selecting models for study.

The most direct way of determining the nucleic acid is to examine the purified particle, but this is probably also the most lengthy, as some viruses, particularly the small thermolabile ones, are difficult to purify. Fortunately, there is at least one apparently conclusive and fairly direct short cut. This is to obtain the nucleic acid in an infective form susceptible to nucleases (usually as the free acid), and then to determine its sensitivity to the two species of nuclease. This has now been done with poliovirus, encephalomyocarditis, mengo, Eastern equine encephalomyelitis, Semliki forest, West Nile, Murray Valley encephalitis and foot-and-mouth disease viruses among the riboviruses, and polyoma[36] among the deoxyviruses, and also for the DNA-containing bacteriophages T_2 (ref. 37) and $X174$ (ref. 38); some

viruses have so far proved resistant to successful extraction, but may yield to improved techniques.

A more readily applied, if less direct, method[39] is to test the growth-inhibitory effect of 5-fluorodeoxyuridine, which should specifically inhibit DNA synthesis. This compound inhibits growth of a deoxyvirus (vaccinia) but not of a ribovirus (poliovirus), and gives promise of reliable results provided that it can be confirmed with more known examples and that it is used with a host cell which it penetrates successfully (that is, in which it inhibits a known deoxyvirus). This is a very simple test, and there is a strong case for all virus laboratories to run it through their collection of virus strains, as the information to be obtained is of primary importance. A preliminary screening of new clinical isolates, for example, with 20 per cent ether and 5-fluorodeoxyuridine, might speed typing and economize in antisera.

Classification of all Viruses

It is tempting to follow this scheme to its conclusion and include all viruses in the one classification, since superficially plant and bacterial viruses seem separated from animal viruses only by host range. This would have the effect, satisfactory from a structural point of view, of placing all bacteriophages and Tipula iridescent virus alongside the adenoviruses, and plant viruses (for example, tomato bushy stunt virus[40]) with poliovirus; the embarrassment of deciding the correct 'kingdom' for plant viruses which grow in insects (and vice versa) would be avoided. In fact, the fundamental likeness in all biological replications and cellular metabolism makes it nowadays legitimate to question seriously whether the usual separation into plant, animal and bacterial viruses is justified, because this classification may depend only on relatively trivial differences in the virus coating. Convincing evidence of this would be growth of a virus in a host of the 'wrong' kingdom; this might be achieved by unusual manipulative techniques, provided that there is no fundamental impediment. Alternatively, evidence for such an impediment would itself constitute most important information.

Conclusions

In summary, a taxonomy for animal viruses based on type of nucleic acid and essential labile lipid content appears less arbitrary and genetically more stable than those previously suggested, and may provide a useful means of ordering the host of viruses now newly coming to light. The typing of the nucleic acid, a factor of primary importance, is likely to be easier than was hitherto supposed, requiring not very accurate assay procedures but needing some system in which infectivity can be detected; it merits wide consideration. Such a taxonomy might in time include all viruses.

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OBITUARIES

Prof. H. R. Dean

Prof. Henry Roy Dean, professor of pathology in the University of Cambridge since 1922 and Master of Trinity Hall during 1929–54, died on February 13, a few days before his eighty-second birthday.

Head-boy of the School at Sherborne, he gained first-class honours and, later, an honorary fellowship at New College, Oxford. He qualified from St. Thomas's Hospital, and was then elected to a senior demyship at Magdalen College, Oxford. Thereafter, on a travelling fellowship, he worked in Berlin with Wassermann. In 1912, he became professor of pathology and bacteriology at Sheffield; and in 1915 professor of pathology and dean of the Medical School in Manchester. He was appointed professor of pathology at University College, London, in 1922 but, before taking up this post, moved instead to Cambridge as professor of pathology there.

Dean's published contribution to medical research was not voluminous, but it laid solid foundations for much of our present knowledge of immunology. His work on complement continued the classical line of Bordet and Wassermann. His work on the precipitin reaction made a quantitative approach to this subject possible. His description of the pathology of anaphylactic shock in man has not been

surpassed. His realization of the essential unity of the antibody reactions helped to bring order into a confused field. His papers, like those of his great predecessors, are classical in quality, commendable to students.

His second great contribution to medical science was the quality and nature of his teaching. Forty years ago, he was a very great teacher, who insisted on the interdependence of all branches of pathology and medicine. He made his students eager to know more and more about more and more. Pathology he regarded as one great subject, of which bacteriology, immunology, virology, haematology and morbid anatomy were all interdependent parts, and liable to suffer from individual elevation to specialist rank. He taught pathology as the true basis of all medicine and as especially valuable for the insight it gave into normal function. He was, thirty and forty years ago, a brilliant lecturer; but his greatest effect was obtained when demonstrating in the laboratory.

His creation of the Part II and Part I Pathology Triposes in Cambridge has benefited many generations of Cambridge medical graduates, and, through them, the whole of medicine.

As a principal leader in the Cambridge Medical School, as Master of Trinity Hall and, during the two difficult and anxious years which preceded the Second World War, as vice-chancellor, Dean's energies were necessarily devoted chiefly to administration. Outside Cambridge, he had many activities; at various times, and for many years at a time, he was chairman of the council of the Imperial Cancer Research Fund, secretary of the Pathological Society of Great Britain and Ireland, a member of the Royal Commission on the University of Durham. He served on the General Medical Council as representative of the University of Manchester during 1919–22, and of the University of Cambridge during 1942–57.

He received several honorary degrees—LL.D. of the Universities of Aberdeen and Western Reserve, honorary D.Sc. of the University of Liverpool. He was a Corresponding Fellow of the New York Academy of Medicine.

Dean was no dilletante, but he was well informed on a very wide range of subjects. To accompany him on a wine-buying expedition for the College; or to handle and appreciate some of the silver he had collected; or to inspect his seedling viruses in Trinity Hall; or to climb mountains with him, or swim with him, or to follow the boats in Mays or Lent races, or sit with him on boards and committees, or hear him quote Horace with a conscientiously archaic pronunciation, or just to drop in for a chat with him—these were all memorable experiences, and for the memory of them one is grateful. But one is chiefly grateful for the example of staunch, objective honesty of outlook on everything that came within his ken, and for the irrepressible humour of his commentary on it. An anonymous contributor to *The Lancet* has said "I owe it to him that I have had such an interesting life". Many others would acknowledge the same debt.

In 1908 he married Irene Wilson, who died in 1959, after being his close partner and perfect counterpart throughout a long joint career. Mrs. Dean shared the affection and regard in which he was held by many hundreds of younger people whom they helped, encouraged, guided and entertained.

E. T. C. Spooner

Prof. Jerome T. Syverton

Jerome T. Syverton, whose death occurred on January 28, began an outstanding, active career in microbiology as an instructor in bacteriology at the University of North Dakota in 1928. Born in Courtenay, North Dakota, in 1907, he entered the University of North Dakota in 1923, obtaining the A.B. degree in 1927 and the B.S. degree in 1928. He graduated from Harvard University School of Medicine in 1931, and after an internship and assistant residency in medicine at Duke University Hospital in 1931–32, he became an assistant in pathology and bacteriology at the Rockefeller Institute for Medical Research, New York. There he obtained basic knowledge in virology under the guidance of Dr. P. K. Olitsky, and in 1932 became a member of the faculty of the University of Rochester School of Medicine and Dentistry.

Except for a sabbatical leave in 1942 at Vanderbilt University School of Medicine as visiting associate professor of pathology and bacteriology, Syverton's fundamental and pioneering work involving, for example, tumour viruses and multiple viral infections of single animal cells, as well as the development of his outstanding skill as a teacher and student adviser, was done during 1934–47 while in the Department of Bacteriology at the University of Rochester. For his outstanding research in virology, he received the Lilly Award in Bacteriology and Immunology in 1938. During 1944–46 he was on active duty in the United States Navy as a visiting investigator at the Rockefeller Institute, and member of Naval Medical Research Unit 2 in the Pacific Theatre. In 1947 he became professor and head of the Department of Microbiology at Louisiana State University School of Medicine, and since 1948 had been professor and head of the Department of Bacteriology at the University of Minnesota.

During his academic career Syverton's enthusiastic and vigorous approach to professional life, with simultaneous devotion to his family and friends, set an extraordinary example for students and associates. His graduate and postdoctoral students during twelve years at the University of Minnesota alone numbered more than 65. His productivity as an investigator was remarkable, and during 1957–58 he was recipient of the Commonwealth Fund Award for Creative Work. Eighty-seven articles describing his own work and 119 in conjunction with his students and associates were published between 1933 and 1960. His stature in science and academic medicine was evidenced by his membership of many scientific advisory committees, and his enthusiastic support of science at an international and national level was widely recognized and appreciated. The world's scientific community has lost a creative and productive investigator, the educational community an enthusiastic teacher, the community of his colleagues and associates a true friend, and his family an affectionate and lovable father.

William F. Scherer

Prof. B. Davison

Physicists and mathematicians connected with the British and Canadian atomic energy projects have learned with regret of the sudden death of Boris Davison on January 24, while still a very productive mathematical physicist engaged on problems of neutron transport.

He was born in Gorky on July 10, 1908, and educated in Russia. He graduated from the University of Leningrad in 1931, and was engaged in hydrology for about seven years thereafter. Through his English grandfather he had a tie with England, and when in 1938 he was requested either to renounce British nationality or leave the U.S.S.R. he elected to go to England. He worked for a short period with Prof. L. Rosenhead, but his health broke down. After a considerable period of convalescence he joined the atomic energy research team at the University of Birmingham under Prof. R. E. Peierls, in 1942. His powers as a mathematician enabled him to make many important contributions, particularly to neutron transport theory, a subject which was to occupy most of his attention for the rest of his life. For some of this work he was awarded the Ph.D. of the University of Birmingham in 1944.

His connexion with Canada started when he joined the Montreal Laboratory of the joint United Kingdom-Canadian Atomic Energy Project in 1943. His association with the late Dr. G. Placzek was a very fruitful one, and he accompanied Drs. Placzek and Mark to Los Alamos. He moved to the new Chalk River Laboratory as a member of the United Kingdom staff in the Theoretical Physics Branch and in 1947 returned to England to work at Harwell. In 1954 he joined the staff of the Computation Centre in the University of Toronto, lectured in numerical analysis and reactor physics and was appointed associate professor of physics in 1960. For the past six years he served Atomic Energy of Canada, Ltd., as a consultant. His knowledge, experience and talent have contributed in many ways to the technical success of the Canadian Atomic Energy programme.

In 1957 his book on *Neutron Transport Theory* was published: it established him publicly as the authority in this subject to which he brought a remarkable combination of analytical power and precision, an uncommon facility in numerical analysis and physical perception. Not only has he expounded the methods of other mathematicians but he has also delineated carefully the boundary of the region within which they can be effectively applied. In his preface he was generous in acknowledging assistance, but those who knew him know well his patience and the exacting standards he set for himself.

Much of Davison's work was concerned with improving mathematical representation of nuclear processes in reactors and with the associated computational problems. He was a ready inventor of algorithms for computing and for avoiding pathological conditions in large calculations.

He was a gentle, shy man, painstaking, kind and generous in helping his fellows, but intolerant of pretence. His intellectual life was not confined to the subject of his specialty. He had a broad, modern interest in science and he liked poetry.

He is survived by his wife Olga.

W. H. Watson

NEWS and VIEWS

The First Manned Earth-Satellite, 1961γ

The spaceship-satellite *Vostok*, launched from the U.S.S.R. at 06.07 U.T. on April 12, carried the first man to make a journey in orbit about the Earth, Major Y. A. Gagarin of the Soviet Air Force. The satellite, which weighed 4.725 kgm. (10,417 lb.) excluding the final-stage rocket, was projected into an orbit inclined at 65° 04′ to the equator, and having an orbital period of 89·1 min. Its height above the Earth varied between 175 km. at perigee and 302 km. at apogee. The satellite, designated 1961γ1, made one revolution about the Earth: its deceleration by retro-rocket motor began at 07.25 U.T. and the cabin was safely and successfully brought to Earth in the U.S.S.R. at 07.55 U.T., close to the pre-determined area. The satellite's radio transmissions were on frequencies of 9·019, 20·006 and 143·625 Mc./s. It is reported that on his historic flight Major Gagarin was able clearly to see coastlines, mountain ranges and large cities, and that to him the Earth appeared light blue in colour against a very dark sky. The final-stage rocket, 1961γ2, which separated from the satellite, remained in orbit for several days.

The Henry Draper Medal : Dr. M. Schwarzschild

Dr. Martin Schwarzschild, professor of astronomy, Princeton University, has been awarded the Henry Draper Medal of the U.S. National Academy of Sciences for his work in the field of stellar evolution. Dr. Schwarzschild was born in Potsdam, Germany, in 1912, and took his Ph.D. degree in astronomy at the University of Göttingen in 1935. He was a Research Fellow at the University of Oslo during 1936–37 and at Harvard College Observatory during 1937–40.

Major Yuri Alekseyevich Gagarin

In 1940, he went to Columbia University as a lecturer on astronomy and was appointed assistant professor in 1944. Joining the faculty of Princeton University in 1947 as a professor of astronomy, he was appointed to the Eugene Higgins chair of astronomy in 1950. Dr. Schwarzschild is widely known as the director of the Project Stratoscope, in which the surface of the Sun was photographed from an unmanned balloon some fifteen miles above the Earth's surface. Analysis of the data obtained from these photographs contributed much towards the understanding of the mechanisms of heat transfer from the centre of the Sun to its surface. For this work Dr. Schwarzschild and two of his colleagues received the Newcomb Cleveland Prize of the American Association for the Advancement of Science in 1957. Also of great importance are Dr. Schwarzschild's computations of the evolutionary track of stars and his study of their internal composition. He is a faculty member of Princeton's James Forrestal Research Center Program in Advanced Physics, and a member of the U.S. National Academy of Sciences.

Theoretical Physics at Birkbeck College : Prof. D. Bohm

Prof. David Bohm, whose appointment is announced to the new chair of theoretical physics at Birkbeck College, London, is well known among physicists as the originator of the Bohm–Pines theory of collective motions in a plasma. He is known to a wider public for his views on the philosophy of science, particularly his criticisms of the interpretation of quantum theory advocated by the school of Niels Bohr. Prof. Bohm, who was born in the United States, was educated at Pennsylvania State College, California Institute of Technology, and the University of California. During the Second World War he worked (for the U.S. Atomic Energy Project) on the electromagnetic separation of isotopes. After the War he became assistant professor at Princeton, and later professor successively at Sao Paulo, Brazil, and the Technion, Haifa, Israel. Since 1957 he has been on the staff of the University of Bristol. He is a physicist of great inventiveness and imagination, whose stimulus and leadership have set several others on the pathway to success in theoretical physics.

Harvard Museum of Comparative Anatomy

Prof. Ernst Mayr has been appointed director of the Harvard Museum of Comparative Zoology as from July 1. Founded by the great nineteenth century naturalist Louis Agassiz, the Museum is one of the very few major centres of natural history research in the United States. The present director, Dr. Alfred S. Romer, who has guided for the past fifteen years the Museum's growing eminence as a centre for the study of animal life, past and present, will continue to teach and do research at Harvard. Both Romer and Mayr hold Alexander Agassiz professorships at the Museum. Prof. Mayr has made important contributions to evolutionary theory during the past thirty years.

Staff College for Further Education

Mr. W. J. Richards, director of the Royal Radar Establishment, Malvern (see *Nature*, **172**, 277; 1953), has been appointed the first director of the proposed new Staff College for Further Education by the Governing Body, set up by the Minister of Education last autumn under the chairmanship of Lord Fleck. Mr. Richards will take up his new appointment in July. The aim of the College is to create a national centre at which principals and other selected staff from colleges of technology and commerce can exchange ideas and experience with senior staff from industry, local and central government, the universities and overseas, and where they can jointly study the aims, ideas and the growth of education in the light of the rapid advances in science and technology. A capital fund of £100,000 has been contributed by industry to meet the initial expenses of founding the College, and the Minister of Education has undertaken to contribute an annual grant towards the running expenses. The College is to be entirely residential and a search is being made for suitable premises, preferably in the Midlands, around which the College can be developed.

Harkness Fellowships of the Commonwealth Fund

The following have been included in the recent appointments to Harkness fellowships of the Commonwealth Fund: J. N. Ball (Liverpool), zoology; J. P. Cornford (Trinity, Cambridge), sociology; J. E. Everett (Clare, Cambridge), geophysics; B. M. Funnell (Trinity, Cambridge), oceanic geology; J. V. Greenman (Gonville and Caius, Cambridge), theoretical physics and applied mathematics; J. M. Hollis (New College, Oxford), philosophy; D. H. P. Jones (Christ's, Cambridge), astronomy; M. C. Scott (Birmingham), nuclear physics; J. J. Turner (King's, Cambridge), infra-red spectroscopy; E. G. Wilson (King's, Cambridge), physics. The following were included in the awards from Australia and New Zealand: N. Sneath (Melbourne), engineering; J. J. Veevers (Sydney), geology. Ten fellowships have been awarded to candidates from France, Italy and the Netherlands.

Commonwealth Students in British Universities

In a written answer in the House of Commons on April 11, Mr. B. R. Braine, Joint Under-Secretary of State for Commonwealth Relations, stated that in July 1959, 3,457 students from the Commonwealth overseas were studying, in United Kingdom universities, the applied sciences to which paragraph 55 of the report of the Commonwealth Education Conference relates. In the academic year 1959–60, this number was 3,338, but figures for 1960–61 are not yet available. More places are expected to become available for such students as the total number of places in United Kingdom universities increases, but the exact number of additional places which would be taken up in 1961–62 cannot be forecast. In 1958–59, 177 students from the Commonwealth overseas were enrolled for full-time research at United Kingdom universities in agriculture and forestry; 130 in dentistry; 1,475 in medicine; 1,608 in technology; and 67 in veterinary science; for 1959–60, the corresponding figures are: 202; 145; 1,477; 1621; and 93. On April 13 a written answer by the Minister of Education, Sir David Eccles, gave the number of Commonwealth students in colleges of further education in England and Wales as 7,203 in the current session, compared with 6,493 in 1959–60. In the present session, the number of Commonwealth students in technical colleges is 477, an increase of 25 on 1959–60.

Employment of Scientists in Government Services

Most of the March issue of *State Service*, the journal of the Institution of Professional Civil Servants, is occupied by the annual report of the Association; but the general secretary, Mr. Stanley R. Mayne, directs particular attention to the difficulty experienced by the Ministry of Aviation in filling posts at principal scientific officer-level as an example of the reluctance of scientists to enter the Scientific Civil Service. The press advertisements only produced five applications, and only one of these was judged worth interviewing, and he was not good enough to be selected. The Department had four other candidates, of whom three were selected and offered appointment but the only applicant from industry declined the offer. Three other scientists were afterwards interviewed and two were selected; one of these has already resigned. The annual report for 1960, which records a membership of 53,923, quoting the figures for recruitment of scientists from the recent report of the Civil Service Commission which are causing the Commissioners grave disquiet, is critical of the value of information collected by the Civil Service Pay Research Unit other than as a broad basis for discussion.

Valuation and Rating of Scientific Institutions

The annual report for 1960 of the Parliamentary and Scientific Committee (Pp. 22. London: Parliamentary and Scientific Committee, 1961) contains a concise summary of the addresses and discussions during the year and of Dr. J. Killian's speech at the annual luncheon. It refers also to the European Parliamentary and Scientific Conference sponsored by the Committee, with the financial support of the Council of Europe, the Organization for European Economic Co-operation and the Foreign Office, in London, during March 21–23, 1961. The Rating Sub-Committee has again considered the position of scientific societies, and at a meeting on December 5 it was agreed to seek amendments to the Rating and Valuation Bill to secure that hereditaments given mandatory 50 per cent rating relief under clause 8 (1) include all hereditaments properly established for scientific purposes, and that the power given to rating authorities to reduce or remit the payment of rates chargeable in respect of such premises should be transferred to the Ministry of Housing and Local Government so that there should be central decision. It was also agreed to seek similar mandatory 50 per cent relief for all organizations qualifying for freedom from income tax under section 449 of the Income Tax Act, 1952 (relating to research associations).

Smithsonian Institution

The annual report for 1960 of the United States National Museum is as usual a well-illustrated, bulky volume giving details of much curatorial work, an impressive account of research undertaken by, or in collaboration with, the staff, and a list of donors and their gifts covering nearly 2,500 accessions (Pp. vi + 175. Washington, D.C.: Government Printing Office, 1960). The modernization programme started about a decade ago continues in all departments, and the construction of the Museum of History and Technology is in progress and will be completed by March 1962. The building has been designed so that the collections will be shown under the best known modern conditions, and also maximum flexibility within the structure for future development has been a prime consideration. In geology events such as the development of jaws and the transition of life from water to land have been demonstrated by diagrams and models. Among the unusual specimens displayed are a 14-ft. skeleton of the predatory Cretaceous fish *Xiphactinus*, and a slab from New Mexico showing the crowded bones of the amphibian *Buettneria*, entrapped in an evaporating Triassic swamp.

The British Leather Manufacturers' Research Association

The annual report for 1959–60 of the British Leather Manufacturers' Research Association records a membership of some 75 per cent of the productive industry with a net increase in membership of 15 and a total income of £70,134, including a grant of £21,900 from the Department of Scientific and Industrial Research (Pp. 70. Egham, Surrey: British Leather Manufacturers' Research Association, 1960). An effluent liaison officer and assistant analyst have been appointed to recommend and demonstrate modifications in leather-making processes designed to reduce effluent problems, and a new radioisotope research laboratory has been built, particularly for the study of chrome complexes in leather by radioisotope techniques. The report of the Director of Research refers to the maintenance of fundamental research on the constitution and properties of collagen and other constituents of hides and skins, the chemistry of vegetable tanners and the mechanical and elastic properties of collagen and leather fibres. In the enzyme unhairing of hides a bath-treatment at 80° F. for three days ensured consistent removal of short hairs with the long hairs, and small-scale trials indicate that no great difficulties should be experienced in vegetable tanning. An investigation of the factors in chrome-tanning processes which are important for satisfactory dyeing has commenced, and the leather properties which are required for good acceptance of pigment finish and good coverage are being investigated; investigations are being made on suede leather with the view of improving the colour fastness, particularly of black suede. Work on the adaptation of semi-chrome upper leather for moulded-sole footwear continued, but mechanical engineering work was discontinued and engineering work will be limited to chemical engineering topics, including effluent problems. Work on the deterioration of leather by heat, moisture and perspiration has led to substantial advances in an understanding of the deterioration of leather by perspiration; but in work on waterproofing of leather the study of laboratory testing methods now has priority, and an extensive testing programme in connexion with sheepskins and sheepskin leathers has been necessary. Besides outlining the programme of research, the report includes a list of publications during the year.

The Cawthron Institute

The annual report for 1959–60 of the Cawthron Institute, Nelson, New Zealand, records some changes in the scope of the Institute's research activities, and its facilities for investigating the more fundamental aspects of plant nutrition have been extended by new equipment (Pp. 35. Nelson, N.Z.: Cawthron Institute). The Director's report reviews the progress

of pasture research, hop research and tomato research at the Institute and of the chemical investigation on the constituents of the tobacco leaf responsible for variations in quality. Besides a list of publications, the report includes five short special articles. E. T. Chiltendon describes investigations on bitter pit in apples; E. B. Kidson, chemical investigations on tomato plants in water culture; D. J. Stanton, further experiments on the treatment of tomato seedlings with *n*-*m*-tolylphthalamic acid; T. B. C. Christie, the effect of fertilizer applications on the *Phytophthora* disease of hops; and R. J. Monk, work on alkaloids and smoking quality of tobacco.

The Brotherton Library, Leeds

The annual report of the Librarian of the University of Leeds, for the session 1959–60, records holdings at July 31, 1960, of 479,157 volumes and 179,215 pamphlets, of which 334,099 volumes and 117,306 pamphlets are in the Brotherton Library (Leeds: The Brotherton Library, The University. Pp. 12. 1960). Accessions during the year totalled 15,842 volumes, 3,281 pamphlets and 31,907 periodical parts. Loans to readers numbered 116,739 and inter-library loans 1,814 books borrowed and 3,449 lent. The report refers briefly to the extension of the Brotherton building proposed in the University Development Plan published in May 1960 which contemplates incorporation of an additional book-stack for 400,000 volumes, together with further reading rooms and larger administrative quarters, and a separate building for undergraduates with space for 800 readers and 30,000–50,000 volumes. The proposals are being studied and, meanwhile, a further investigation of undergraduate use of library services is being made.

Raw Materials of Ceramics

In *The Museums Journal* of March 1961, Mr. P. J. Adams describes an exhibition which was arranged to mark the occasion of the Seventh International Ceramic Congress and suitably modified will form a permanent feature at the Geological Survey and Museum, London. The exhibition is divided into three sections reflecting the main branches of the British ceramic industry: (1) pottery and whiteware; (2) structural clay-products; and (3) refractories and technical ceramics. Each section consists of a simple wall-type display with a single waist-high bench for the geological and ceramic specimens and a back-screen for narrative text, geological maps, photographs and diagrams. The nature, geological occurrence and methods of exploitation of the raw materials are briefly described and their processing and utilization are summarized.

Selenium Poisoning

Selenium poisoning is known to be a disease of domestic animals in the United States. Wheat, corn and milk produced in western and southern districts of the United States contain small quantities of selenium. Animal and vegetable foodstuffs from the United States make up an increasing part of the diet of Japanese school-children and this has led to investigations into experimentally produced selenium poisoning in various animals (*Yokohama Med. Bull.*, 11, No. 5; October 1960). The investigations were carried out by Hiroshi Tsuzuki, Kazuhoshi Osawa and Takashi Hosoya of the Department of Hygiene, Yokohama University School of Medicine, Yokohama, and showed that selenite had the greatest toxicity among animals. It disturbed the body weight, tibial length and physical strength of animals when it was given intraperitoneally and orally. Inhaled selenium vapour disturbed physical functions, but the toxicity varied because of varying degrees of selenium in the air. Metallic selenium, which was given orally, disturbed digestive functions temporarily and greatly influenced gain in weight and physical strength; it suppressed the development of tibial length only slightly. Selenium in ointment, rubbed on the skin of animals, caused a remarkable dermatitis, and a decreased gain in weight, but there was only slight suppression of tibial length and physical strength. Generally, females were more disturbed physiologically and developmentally than males. The second generations which were born from poisoned mothers seemed to have higher resistance to selenium than other animals.

Internal Carotid Artery Occlusion

In recent years, internal carotid artery occlusion has been diagnosed frequently in young adults. A study by John G. Humphreys of the Department of Medicine, University of Toronto, and T. H. Newton, Department of Radiology, University of California, of seventeen patients of less than 40 years of age with carotid occlusion shows how the underlying mechanism accompanying the occlusion may differ from that in older patients in whom the cause is atherosclerosis (*Brain*, 83, Part IV; 1960). There were thirty-three older patients whose carotid occlusions occurred after the age of 40. There was little difference in the sex incidence of the younger group compared with the predominance of males in the older group. Eleven of the seventeen patients in the younger group either had lesions adjacent to the carotid artery or had evidence of a generalized systemic illness at the time the carotid occlusion was diagnosed. Four of the thirty-three patients of more than 40 years old had similar complicating factors. The complications of both groups included trauma, aneurysm, tumour, pregnancy, and inflammatory diseases. Hypertension, diabetes and atherosclerotic involvement of other major arteries were noted in only one of the seventeen younger patients, but were present in thirteen of the thirty-three older patients. The prognosis for survival following an internal carotid artery thrombosis is better in patients of less than 40 years of age.

Dietary Fats and Cholesterol

In recent years the number of people dying from the sequelæ of vascular diseases has been as great in the Netherlands as highly industrialized countries. The influence of various dietary fats on the blood cholesterol content has been investigated by F. S. P. Van Buchem, J. J. Speelman, A. A. Idema, A. T. Valkema and H. J. Thomasson, and is reported in the recent *Proceedings of the Royal Netherlands Academy of Sciences* (Series C. Biological and Medical Sciences, 44, No. 1; 1961). The twenty test subjects were physically healthy, were mentally defective and were constantly under clinical and dietetic supervision. Before the test diets were given, the spontaneous variations of the serum cholesterol-level of most test subjects were studied for several months. The test diets used only differ from normal diets in that different fats, but in the

same amounts, were given. If maize oil was used as a fat, the serum cholesterol-level fell in all of them, but it rose on cocoa fat feeding. The influence of various mixtures of maize oil and cocoa fat was also studied. The phospholipid content of the blood fell also with maize oil, but not so strongly as the cholesterol-level. The influence on the neutral fat differed in the various test subjects. The cause of this rise or fall of the serum cholesterol-level has not been determined.

New Species of Rotifer

From a pool (*p*H 6·6·5) on Cawston Heath, eleven miles north-east of Norwich, a hitherto undescribed *Collotheca* sp. with only four coronal knobs has been taken occasionally since 1957. This rotifer takes its place in the list with the two four-lobed members of the genus so far recorded, namely, *Collotheca quadrilobata* (Hood) and *C. monoceros* (Zacharius). H. G. S. Wright, in an article appearing in a recent issue of the *Journal of the Quekett Microscopical Club* (Series 4, 5: No. 13: 1961) regards this as a doubtful identification, the description and figure given by Zacharius strongly suggesting a mutilated *Stephanoceros fimbriatus* (Goldfuss). The new rotifer has the following specific characters; the corona is quadrate in plan and its base not wider than the body, with a flattened truncate lobe at each angle and a prominent lip on the ventral edge. There is no dorsal lobe, there are long cilia on the lobes, and on the dorsal and lateral rims of the corona is an inner series of short inactive cilia and an outer series of cilia in constant flagellatory motion. The long foot is frequently four times, or even more, the length of the corona and trunk combined. Wright proposes the name *Collotheca quadrinodosa* n. sp.

The Brandberg and Other Rock-Shelter Paintings of the Union of South Africa

The Abbé Breuil's contention that the Brandberg paintings were of vast antiquity and the so-called 'white lady' a portrait of a European has been hotly contested by prehistorians in South Africa. Some years ago the late Dr. van Riet Lowe suggested that the date could equally well be A.D. 1600 or 1600 B.C. Indeed, nowadays, it is becoming more and more difficult to assign any great age to the rock-shelter paintings in the sub-continent. Revel Mason further points out that though some of the painted individuals seem to show Caucasoid features, such features are common among the southern Bantu to-day. Again, the smearing of white paint on the face for certain ceremonial purposes is not unknown. The physical characters shown in the Tsisab paintings, therefore, give no very certain evidence as to racial type, but the clothing, ornaments, etc., depicted fit in with those found among primitive tribes south of the Zambesi. There is no need to suggest relationship with Cretan or Egyptian originals, or to advocate any very great antiquity for this art. Revel Mason is well known among the younger prehistorians in South Africa. Under the auspices of the Archæological Survey of the Union of South Africa, Pretoria, he has published a pamphlet full of coloured illustrations dealing with his discoveries of a new series of rock-shelter paintings in the Brandberg, south-west Africa and another series at Waterberg, Northern Transvaal. While the whole is only a few pages in length, it is an attractive little work which adds to our knowledge of South African rock-shelter art.

Scientists Working in Antarctica

The Special Committee on Antarctic Research of the International Council of Scientific Unions now maintains a register of scientists wishing to work on Antarctic expeditions of other nations. The Committee is merely acting as a centre which may put suitable scientists from other countries in touch with national committees which can use their services to advantage. Further arrangements for the employment of individuals are then a matter of negotiation between the expedition organization and the person concerned. Men with previous polar experience would be most suitable. Registration forms are available from the Assistant Secretary, Royal Society, Burlington House, London, W.1.

Ford Foundation Grant to the Zoological Society of London

The Zoological Society of London has received a further grant of 95,000 dollars from the Ford Foundation to supplement the grant of 550,000 dollars announced in May 1960. Both these grants have been made to support a programme of research in animal reproduction. The original grant of 550,000 dollars from the Ford Foundation was to endow a series of research fellowships, and the appointments of Dr. Peter Jewell, Dr. Lorna Kellas and Mr. David Kirby to the first three fellowships were announced in February of this year.

Royal Geographical Society Award for Women

As the result of a bequest from the late Lady Dorothy Mills, Fellow of the Royal Geographical Society, an award of £1,000 has been established, to be known as the Lady Dorothy Mills Award. The Award will take the form of a studentship involving some element of adventurous travel or exploration, by land or air, tenable for one or more years within the limits of the sum available. Applicants (of any nationality) must be women over twenty-one and preferably under the age of thirty years. They must be Fellows of the Royal Geographical Society. The study which forms part of the candidate's programme may be in any field of science or the humanities, provided that it has some geographical content or aspect. Further information can be obtained from the Director and Secretary, Royal Geographical Society, 1 Kensington Gore, London, S.W.7. Applications must be submitted by February 12, 1962.

International School for Research and Education in Physics

An international school for research and education in physics has been established at the University of Uppsala. The school is being jointly sponsored by the International Atomic Energy Agency, the United Nations Educational, Scientific and Cultural Organization and the Central Committee for Swedish Technical Assistance. The school is offering one-year courses, the first of which will start on September 1 and finish about July 1, 1962. The aim of the school is to provide possibilities for individual participation in qualified experimental research work in one of the various fields of physics under experienced guidance. The school is open to participants from all countries and a number of fellowships will be available. Further information can be obtained from the International Seminar, Institute of Physics, University of Uppsala, Uppsala, Sweden.

National Agricultural Advisory Service

Recent changes in the National Agricultural Advisory Service include the following: Mr. J. Butt-Evans, at present county advisory officer for Durham, to be county advisory officer for Yorkshire (North Riding), in succession to Mr. W. S. Rayfield, who was recently transferred to headquarters; Mr. G. P. Chater, at present hops adviser in the West Midland Region, to be director of the Rosemaund Experimental Husbandry Farm, Preston Wynne, Hereford, in succession to Mr. E. L. Jones, who succeeds Mr. W. R. Smith as one of the two livestock husbandry officers for Wales.

American Geophysical Union: Officers

The triennial elections of the national officers of the American Geophysical Union have recently been held, and the following have been elected for a three-year period from July 1: *President*, Dr. Thomas F. Malone, director of research, Travelers Insurance Co., Hartford, Connecticut; *Vice-president*, Dr. George P. Woollard, professor of geophysics, Department of Geology, University of Wisconsin; *General Secretary*, Dr. A. Nelson Sayre, senior scientist, U.S. Geological Survey, Washington, D.C.

The Night Sky in May

New moon occurs on May 14d. 16h. 55m. U.T. and full moon on May 30d. 04h. 38m. The following conjunctions with the Moon take place: May 6d. 12h., Saturn 3° S.; May 7d. 00h., Jupiter 3° S.; May 11d. 16h., Venus 4° N.; May 20d. 18h., Mars 4° N.; May 22d. 13h., Regulus 0·7° N. In addition to these conjunctions with the Moon, Mercury is in conjunction with Aldebaran on May 15d. 22h., Mercury being 7° N. Mercury is an evening star, and is visible in the west after sunset; on May 31 it sets about two hours after the Sun. Venus is a morning star, but it is too close to the Sun for easy observation. Mars is an evening star, but conditions for observation are becoming less favourable. It sets about midnight; its stellar magnitude is + 1·5 on May 15, and its distance from the Earth on May 15 is 158 million miles. Jupiter rises at 1h. 40m., 0h. 50m. and 23h. 45m. on May 1, 15 and 31, respectively. It is in Capricornus, its stellar magnitude on May 15 is − 2·0 and its distance from the Earth on that date is 440 million miles. Saturn rises at 1h. 20m., 0h. 45m. and 23h. 20m. at the beginning, middle and end of the month, respectively. It is near the border of Sagittarius and Capricornus; on May 15 its stellar magnitude is + 0·7 and its distance from the Earth is 890 million miles. There is one occultation of a star brighter than magnitude 6 visible at Greenwich; May 2d. 23h. 16·6m., 24 Sco., reappearance.

Announcements

Prof. Jean Brachet (Brussels) and Prof. Hans Bauer (Wilhelmshaven) have been awarded the Schleiden Medal of the Leopoldina German Academy of Science, for their outstanding work in the field of cytology.

Dr. B. P. Pal, director of the Indian Agricultural Research Institute, New Delhi, has been awarded the first Rafi Ahmed Kidwai Memorial Prize of the Indian Council of Agricultural Research, for his work on the breeding of Pusa wheat varieties.

Mr. E. S. Calvert and Mr. J. W. Sparke, both of the Ministry of Aviation's Royal Aircraft Establishment, Farnborough, have been awarded the 1961 Laura Taber Barbour Air Safety Award, in recognition of their "major contribution to world air safety through joint development of the Line and Bar Approach Lighting System and the Visual Glide Path Indicator now installed and in use at many major airports". The Award is made annually by Flight Safety Foundation Award Inc., of the U.S. Society of Automotive Engineers Inc.

The Duke of Edinburgh will open the McFadzean Laboratory at the Wood Lane research centre of British Insulated Callender's Cables, Ltd., on May 16.

The Bradford Institute of Technology is organizing a special short course on "Methods of Polymer Characterization and Analysis" during June 23–24. Further information can be obtained from the Registrar, Institute of Technology, Bradford 7.

The Biology Department of Brookhaven National Laboratory is organizing a symposium on "Fundamental Aspects of Radiosensitivity" during June 5–7. Further information can be obtained from Dr. A. H. Sparrow, Brookhaven National Laboratory, Associated Universities Inc., Upton, L.I., N.Y.

The Applied Spectroscopy Group and the Manchester and District Branch of the Institute of Physics and the Physical Society are holding a joint one-day meeting on "Spectroscopic Studies using Time Resolution Techniques", on June 16. Further information can be obtained from the Institute of Physics and the Physical Society, 47 Belgrave Square, London, S.W.1.

The International Academy of Astronautics of the International Astronautical Federation is organizing a symposium on "Space Flight and Re-entry Trajectories" to be held in Paris during June 19–21. A number of symposia are planned, dealing with the following subjects: trajectories for lunar and interplanetary missions; orbital transfer and rendezvous; near-Earth satellites; dynamics of terminal re-entry. Further information can be obtained from the International Academy of Astronautics, 12 Rue de Gramont, Paris 2e.

The British Biophysical Society is organizing a meeting at the University of Nottingham during July 26–28. Two symposia are being organized: "Phloem Transport in Plants" and "Electron Transfer in Biological Molecules". There will also be a session for the reading of papers, and a discussion on "International Organization in Biophysics". Further information and application forms can be obtained from the honorary treasurer, Dr. P. M. B. Walker, Zoology Department, University of Edinburgh, West Mains Road, Edinburgh.

An informal meeting is to be held at the Royal College of Science and Technology, Glasgow, on June 27, under the auspices of the Faraday Society, to mark the centenary of the publication by Thomas Graham of his paper on liquid diffusion, in which he distinguished between colloids and crystalloids. Mr. D. C. Henry, of Manchester, will preside, and speakers will include: Sir Eric Rideal, Prof. J. A. V. Butler, Dr. A. S. C. Lawrence and Dr. A. P. Prosser. Further information may be obtained from Dr. A. J. Hyde, Department of Chemistry, Royal College of Science and Technology, George Street, Glasgow, C.1.

THE BELGIAN ADVISORY COUNCIL FOR SCIENTIFIC POLICY

THE Belgian Advisory Council for Scientific Policy was established by a royal decree of September 16, 1959, which also established a Ministerial Committee of Scientific Policy and an Inter-departmental Commission of officials. The Council, of which Prof. L. Massart is chairman and Prof. M. Dubuisson vice-chairman, is to study, in close co-operation with the universities and equivalent institutions of higher education, the development of these institutes commensurately with the nation's needs and make appropriate proposals, as well as the extension of research; to maintain records of the nation's research services and their work; to propose ways of promoting and co-ordinating scientific research in both the economic and the academic sector; to formulate an overall programme for the expansion of research, and to suggest appropriate means of financing scientific research; to study conditions determining efficiency in research and methods of co-ordinating the application of results; and to advise the Government on Belgian participation in international scientific activities. The Council is assisted by two standing committees, an Industry–University Liaison Committee and a Committee of Scientific Experts, and it has already established working parties on medical research and agronomic research.

The Council's first annual report covers the period September 1959–September 1960, in which the broad lines of an overall programme are first outlined, while in the second part of the report the Council's operations are surveyed and in particular the recommendations it has already made (Pp. 132. Bruxelles: Conseil National de la Politique Scientifique, 1960). The first aim of scientific policy is seen as the development of scientific research and the training of manpower for this purpose, and it is the task of the Council to define with sufficient accuracy the objectives of scientific policy and the means to be used to achieve them in the light of economic policy and resources. This involves the submission of recommendations regarding man-power, institutions and resources, and the report considers in some detail the adaptation of the equipment of Belgian universities to the new needs arising in university expansion and the adaptation of methods of teaching and training.

The Council is particularly concerned about the problems of a reasonable balance between the numbers of young people trained for particular occupations and the number of appropriate openings. As regards institutions, the Council has already endorsed the findings of the National Science Commission, which proposed a five-year plan for expanding the universities' scientific, technological and administrative man-power, higher subsidies for the non-State universities and a plan for expanding the State universities. Certain fundamental reforms in university curricula are put forward as urgent, and a University–National Council Liaison Committee has been established. The Council has also urged recommended implementation of plans recently drafted for expanding the staff of scientific establishments under the Ministry of Education. With regard to finance of scientific research, the Council has recommended the appropriation of 75 million francs, to be allocated progressively during 1961 to new projects as they appear desirable.

Discussing international aspects of scientific policy, the report stresses the importance and efficacy of international co-operation in research, as in the European Nuclear Research Centre, and particularly its value to the smaller countries. Finally, the problem of scientific institutions in the Congo is briefly discussed.

THE WOOL INDUSTRIES RESEARCH ASSOCIATION

NEW LABORATORIES FOR WORSTED PROCESSING

THE new Worsted Processing Block at Torridon, the Leeds headquarters of the Wool Industries Research Association, was opened by the Right Hon. R. G. Menzies, Prime Minister of Australia, on March 22.

Both the chairman of the Association, Mr. Basil A. Smith, and the director of research, Dr. A. B. D. Cassie, have long been concerned with the development of worsted processing research at Torridon. Mr. Smith has been very active in the Association's affairs since 1929, particularly in the field of scouring and combing, and also in that of finance—an important aspect when new projects are planned. Dr. Cassie joined the staff of the Association in 1938 as head of the Physics Department and was appointed director of research in 1950. Much of his own work has been of direct and indirect importance to the worsted industry; for example, his researches on the flow of air through porous plugs led to the development of the Association's fibre fineness meter, now widely used in the industry.

Early Researches

The programme of work being undertaken in the new laboratories inevitably stems from earlier fundamental and applied researches relative to the processes concerned: scouring and drying of loose wool, carding, combing, drawing and spinning. In 1920 very little was known about the physical properties of the wool fibre. The general principles of the exchange of moisture between wool and the ambient atmosphere were understood; and there were methods for measuring the moisture content of wool. But virtually nothing was known about the effect of the moisture content of wool at the various stages of processing, how it changes during processing, and how the moisture content is affected by the relative humidity of the atmosphere. These subjects have been thoroughly investigated, and the findings are now applied in the industry. The first testing room with controlled atmosphere was set up at Torridon; the method used, that of wetting

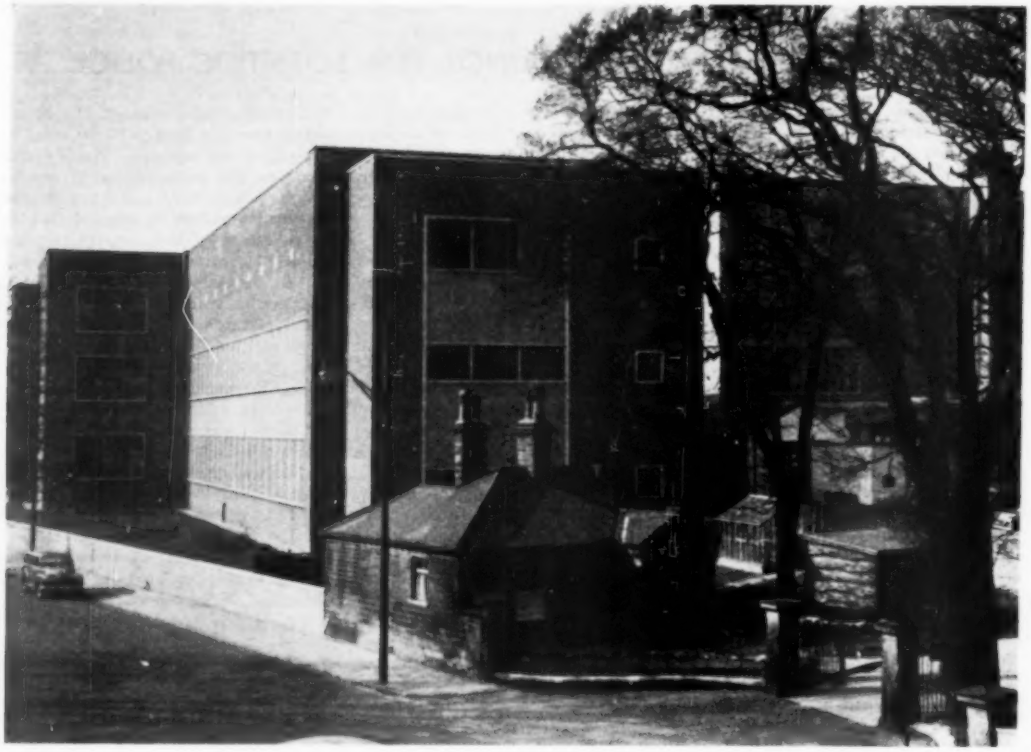

Fig. 1. The new Worsted Processing Block at Torridon, Leeds

and drying towers, was later adapted for commercial control cabinets.

Before 1920, although the industry used several methods for combating the effects of static electricity, little was known about its cause. This phenomenon was studied, therefore, and the findings indicated that the most effective way of dealing with 'static' is to attack it at its source. This knowledge has been used by chemical manufacturers in the development of anti-static dressings for use on wool during processing.

Scouring

The change of *p*H in the liquors during scouring, the use of various alkalis, and the scouring properties of suint (exudation from sweat glands of the sheep) have all been investigated at Torridon since the early 'thirties. In 1953 a complete scouring plant was installed and has now been transferred to the new Worsted Block. Recent research work has led to a greater understanding of the physico-chemical mechanism of scouring, and of the mechanical action. It has been shown that most of the mechanical scouring action takes place not in the bowls but at the point where the liquor is expressed by the squeeze rollers. This type of research has involved the devising of methods for separating and measuring the constituents of the liquors: grease, soap and free fatty acids.

Carding and Combing

The avoidance of fibre breakage is an important requirement in the early stages of worsted yarn production. Investigations have shown that fibre breakage in worsted carding depends largely on the state of the wool coming from the scouring. This finding has stressed the desirability of a gentle mechanical action in scouring. The modern type of air-flow dryer through which the wool passes after scouring, using the principles advanced by the Wool Industries Research Association in 1938, also does much to lessen the entanglement of the fibres.

Progress in methods for the removal of burr (vegetable matter) in carding had at one time been hampered by the difficulty of estimating the amount of burr in a sample. Satisfactory mechanical and complementary chemical methods of estimation have now been developed and the requirements for efficient burr removal are consequently more thoroughly understood.

Research in combing is being directed to the improvement in the thickness regularity of the combed sliver, this having increased in importance with the introduction of the new drawing and spinning techniques mentioned here.

Drawing and Spinning

About eight or ten stages of attenuation had been traditionally used in drawing 'tops' (the product of the comb) to the 'roving' from which the worsted yarn is spun. The development of the Association's roving levelness tester and the early work on roving and yarn irregularity led to the introduction of shorter processes by many firms. An outcome of

this line of advance was the invention of the Raper autoleveller, a drawing machine which maintains thickness regularity by automatically taking account of the irregularity of the ingoing material. Mr. George Raper brought his idea to Torridon for early development, and after further development in a mill it was put into commercial production. This system of drawing, in conjunction with the Ambler 'superdraft' system of spinning (developed by Mr. Geoffrey Ambler with the co-operation of the University of Leeds), is now accepted as one of the modern methods of worsted drawing and spinning.

A more recent achievement, used as a part of a shortened drawing system, is the Association's rotating can system, in which twist is inserted by means of a rotating can instead of a spindle. Other investigations in improved methods of worsted drawing are being pursued at Torridon, including the use of closed loop servo-techniques for auto-levelling.

An important aspect of the irregularity of the ultimate yarn is its effect on the appearance of the fabric. The Association has pioneered the expression of this irregularity in numerical form, and the problem of linking numerical assessment with visual judgment is still being studied.

Many other projects are in hand, both in scouring and combing and in drawing and spinning. Members' day-to-day problems often lead to some profitable line of research the solution of which benefits the industry as a whole. The use of man-made fibres in blends with wool raises difficulties at various stages of processing. New types of machinery introduce new aspects of old ones. This kind of service to the industry will be greatly facilitated by the increase of machinery and laboratory space in the new Worsted Block.

H. LEMON

APPLICATIONS OF INTERFERENCE MICROSCOPY

A SYMPOSIUM on this subject was held at the Royal Microscopical Society's London headquarters on March 15. The president, Dr. V. E. Cosslett, was in the chair and the audience included a number of visitors from abroad. It is nearly ten years since the first interference microscopes suitable for general use began to appear, and the purpose of the meeting was to take stock of the present position and to review some of the main applications of the instrument in various fields.

In his introductory survey Dr. R. Barer (Oxford) dealt with the instrument, theory of operation and the principles underlying its use for 'weighing' cells. He paid tribute to the work of J. Dyson, F. H. Smith and J. St. L. Philpot, who made the development of modern high-aperture instruments possible, and discussed some of the problems common to all types of interference microscope. The operation of a two-beam interference microscope can be explained by means of a simple vector theory which shows how the optical path difference produced by a transparent specimen can be measured and also demonstrates the similarity between interference and phase-contrast microscopy. The latter can be regarded as a form of interference microscopy in which the two interfering beams are imperfectly separated. This causes the edge of a refractile object to be surrounded by a halo and the contrast of edges and discontinuities is accentuated. These apparent defects of phase contrast are not necessarily a disadvantage for purely observational work; and the image of a cell seen through an interference microscope is often disappointingly 'flat' and lacking in internal contrast as compared with a phase-contrast image. Dr. Barer concluded by giving a practical interpretation of the meaning of optical path difference, the quantity normally measured with an interference microscope. The refractive index of a solution varies linearly with its concentration and since the optical path difference is defined as the product of the object thickness and the difference in refractive index between the object and the surrounding medium, it follows that the optical path difference is proportional to the dry mass per unit area. This is an important quantity in cytology, but present methods are mainly adapted to point-by-point measurements and the integration of dry mass over the area of a cell might be very tedious. The full value of interference microscopy in biology will not be realized until automatic integrating devices, based on rapid electronic scanning and capable of 'weighing' a cell in a fraction of a second, have been developed. This is a technical problem and by no means insoluble.

Dr. K. F. A. Ross (Leyden) described how interference microscopy can be used to measure the mass or solid concentration of cell inclusions. It is necessary to overcome the difficulty that the inclusion is surrounded by a layer of cytoplasm of unknown thickness. One method is to immerse the cell in an isotonic protein solution having the same refractive index as the cytoplasm. The difference in refractive index or concentration between the inclusion and the cytoplasm can then be found. Measurements of this type have been made on the Nebenkern of the locust spermatid, a body formed by the fusion of mitochondria. Values in the range of 21–26 per cent for solid concentration were obtained. Work on lipid droplets in various cells has thrown some light on their physical state. The refractive index of droplets known to contain mainly phospholipids is considerably lower (about 1·42) than that of any pure lipid substance. This suggests that in their natural state these bodies are highly hydrated, a conclusion supported by evidence from polarization and electron microscopy. Finally, Dr. Ross described measurements on different regions of the giant salivary gland chromosomes of *Chironomus*. A number of different methods all showed that the euchromatic regions contained a higher concentration of solids (20–25 per cent) than the heterochromatic regions (10–15 per cent).

Dr. E. J. Ambrose (London) described his work on cell division. The instrument used was a polarizing type of interference microscope with a birefringent wedge mounted in the eyepiece. Time-lapse cine-films in colour were taken of dividing cells, simultaneously with a coloured image of the wedge. The optical path difference of any part of the cell could

be measured by matching its colour against the scale of colours exhibited by the wedge. In some cases it was necessary to compress the cells in order to obtain good optical conditions, but with plant endosperm the cells could be mounted on a thin film of agar on which they were made to spread out by surface tension. Measurements were made on the cytoplasm, nuclear sap, chromosomes, spindle and cell plate. A good correlation was found between regions of high mass per unit area and the development of birefringence. Dr. Ambrose concluded by showing some excellent colour films of cell division.

The three papers in the afternoon session were devoted to non-biological applications. Dr. S. Goldstaub (Strasbourg) first described his work on crystal growth. The interference fringes surrounding a crystal immersed in its mother liquor are in fact lines of equal concentration. In regular growth these fringes tend to cut across the corners of the crystal, so that the crystal surface is not a region of constant concentration. Nevertheless, since the fringes move parallel to themselves during growth, an equal mass of material is deposited over the whole surface. In dendritic growth, on the other hand, the fringes do not cut the crystal surface. Dr. Goldstaub also gave an interesting account of the use of the interference microscope for studying the behaviour of salt solutions surrounding isolated particles of ion exchange resins. The flow of ions from the solution to the resin gives rise to concentration gradients, and hence to fringes around the particles so that the exchange process can be observed directly. A colour film illustrating some of these points was shown.

Dr. R. C. Faust (Imperial Chemical Industries, Ltd., Northwich) discussed the study of optically heterogeneous specimens with special reference to textile fibres. Many fibres are far from homogeneous and some possess a surface layer or 'skin' that differs markedly from the central core. A knowledge of the absolute refractive indices at different parts of a fibre is an important guide to the degree of molecular packing and orientation. A convenient method of observing the variation in refractive index is to immerse the fibre in a liquid of known refractive index and to study the way in which interference fringes are deviated in traversing the image of the fibre. At those points at which the fringe is undeviated the refractive index of the fibre matches that of the liquid. If the refractive index of the liquid is changed by varying the wave-length or the temperature, new match positions are obtained. A map of refractive index variation can thus be built up. In some unstretched fibres the refractive index for polarized light vibrating parallel to the axis remains essentially constant across the fibre whereas for light vibrating perpendicular to the axis the index falls rapidly from the edge to the centre, so that the birefringence is maximal at the edge. After stretching, however, both refractive indices vary together, giving uniform birefringence. Dr. Faust emphasized that the optical properties of fibres vary considerably, depending on the method of manufacture.

A glimpse into the future was provided by the last speaker, M. Marcel Locquin (Paris). He described how microscopes are needed to magnify the very small 'memories' used in machines for automatic documentation and translation. The 'memories' are produced as photomechanical negatives by a process similar to that used for making graticules. Although in most European languages 40,000 phrases are in common use, about 90 per cent of a language can be translated with only 2,000–4,000 phrases. A common word can be represented by one or more letters using speedwriting shorthand. Additional letters are used to represent the dependence of one word on another. The encoded phrases are made into a memory which can be a thousand times smaller than a magnetic type of memory. The memory negative is magnified through a microscope and its enlarged image falls on to a 'question' in the form of a photographic positive. A photoelectric system measures the amount of light transmitted by the overlapping images; if the memory and the question are identical no light is transmitted and various degrees of similarity can be selected according to the light transmitted. Such a system can be used for selecting papers on similar subjects without human intervention. The particular advantages of an interference microscope for this work are that it provides a means of contrast variation and that silver grains in the photographic emulsion are rendered essentially transparent by interference contrast, so that the image is effectively grain-free. However, M. Locquin felt that there were possibilities for reducing the size of the memories still further and looked forward to the day when they would have to be magnified by means of an electron microscope.

R. Bareb

THE CARNEGIE TRUST FOR THE UNIVERSITIES OF SCOTLAND

THE fifty-ninth annual report of the Carnegie Trust for the Universities of Scotland, covering the year 1959–60, includes that of the Executive Committee, the abstract of financial accounts for the year ended September 30, 1960, lists of publications during the year from Fellows, Scholars and recipients of grants, and of papers published by the Royal Society of Edinburgh assisted by Carnegie grants, and the usual reports on the work of Fellows and Scholars and on research grants and travel grants awarded during the year*.

* The Carnegie Trust for the Universities of Scotland. Fifty-ninth Annual Report for the year 1959–60 submitted by the Executive Committee to the Trustees on 27th February, 1961. Pp. iv + 66. (Edinburgh: Carnegie Trust for the Universities of Scotland, 1961.)

In annual and non-recurrent grants in the 1957–62 quinquennial distribution the heaviest items have been more than £18,000 by St. Andrews on the new Biology building, a similar sum by Glasgow on the new Arts building, and more than £23,000 on the new Physical Education Centre; more than £26,000 by Aberdeen on the new hall of residence, Crombie Hall, and nearly £9,000 by Edinburgh on the new hall of residence at Salisbury Green (Holland House). The Committee is now considering its policy with regard to capital grants for the period 1962–67, and has agreed to ask each university, in formulating proposals for use of the Trust's funds in this eleventh quinquennial distribution, to concentrate on projects

which are not supported by the University Grants Committee.

Expenditure on the research scheme has risen to more than £117,000, that on postgraduate scholarships and fellowships remaining about the same. During 1959–60 all four Fellows were in the humanities, but 3 out of 5 Senior Scholars and 31 out of 56 Scholars were in science; 19 Scholars, 3 Senior Scholars and 3 Fellows were new appointments. Of 44 research grants, 13 were towards the cost of illustrating research papers with special diagrams, maps or photographs, and 10 were travel grants of special kinds. Seven major travel awards were made, making a total of 40 over the past three years, and the Committee continues to attach great importance to these foreign travel awards. The policy remains clear-cut: a high standard of research achievement must be established; the journey proposed must be based on the intention to carry out research or acquire new research techniques; and no applications will be accepted where the central purpose is to attend an international conference. Awards in 1959–60 include those to E. W. Fisher for comparative studies of the cardiovascular system of the horse, cow and dog, at Pennsylvania; G. F. Hamilton, for studies of the supplementary motor areas of the primate cortex at Michigan; G. Eglinton, to study chemical constituents of the flora of the Canary Islands; N. A. Mitchison, to study cellular aspects of antibody synthesis at Stanford; and R. G. Moorhouse to study elementary particle physics at the European Centre for Nuclear Research, Geneva.

Only seven authors received subventions towards the cost of publishing books, and while the policy of aid for the Scottish learned societies with the cost of publishing their *Proceedings* or *Transactions* continued, the Committee intends to adhere strictly to its new policy of reviewing applications simultaneously once a year, and imposing a ceiling of £2,500 on such expenditure.

NATURE OF SARCOLEMMA, THE STRIATED MUSCLE FIBRE MEMBRANE

By Prof. F. LORINCZ and Dr. G. BIRÓ

Hungarian Meat Research Institute, Budapest 2

THERE is a close relationship between the structure of muscle tissue and the palatability of meat, above all, its softness, tenderness, and even its biological value (for example, the ratio of true muscle tissue to connective tissue). Among the tissue components of the muscle cells, the structure and function of the sarcolemma have not yet been examined in such detail as those of other components of the muscle cells.

Jones and Barer[1], Rózsa, Szent-Györgyi and Wickoff[2], Conte and Rieser[3] and Wang[4] have investigated the nature of sarcolemma. Jones and Barer failed to confirm the opinion that the sarcolemma is a sheath composed of fine collagenous or reticular fibrils. By means of the electron microscope it was recognized as a fine membrane on which small spots were seen. According to these authors, it is possible that the small spots might be points of attachment of either connective tissue fibrils or myofibrils. Rózsa *et al.* described the sarcolemma as a thin sheet having a granular surface to which threads are attached. According to their view, these threads actually do not belong to the sarcolemma, but rather to the system of fibrils surrounding the muscle fibres. After a critical survey of the assertions of other authors, Conte and Rieser suggested, as a result of their tests, that the sarcolemma is a protein membrane free of a collagenous or fibrillar structure. It is most likely a lipoprotein, and this is in agreement with the fact that also the mammalian erythrocyte envelope is a membrane of this type. Finally, according to Wang's view, the bipartite nature of the sarcolemma can be recognized. The true sarcolemma is a homogeneous membrane about 0·1μ thick, which is surrounded by the fibrous sarcolemmous envelope.

We have also examined the finer structural conditions of muscle, from both chemical and histological points of view[5,6]. For our experiments reported here, we took samples from the gluteus medius of a cow about 3 years old, a quarter of an hour after death. After having freed the samples carefully from the other visible tissue elements, that is, the adipose and coarse components of the connective tissue, the samples were transversely cut up into small pieces measuring about 3–5 mm. in thickness and disintegrated in sterile physiological solution of sodium chloride utilizing a Waring blender. Our purpose was to obtain isolated muscle fibrils.

On examining the disintegrated tissue under a microscope, a phenomenon formerly not experienced

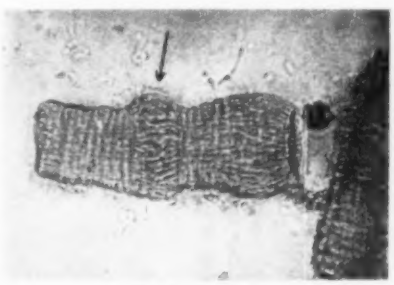

Fig. 1. (× 200)

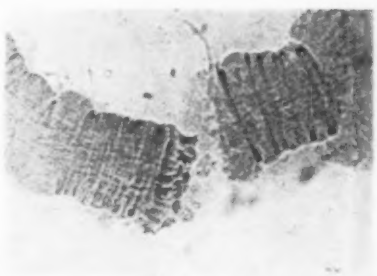

Fig. 2. (× 200)

Fig. 3. (× 200)

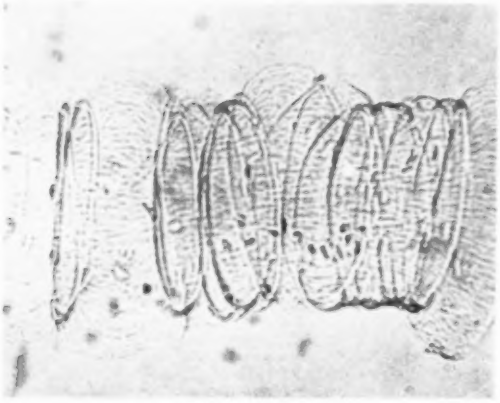

Fig. 4. (× 500)

was seen (Figs. 1–4). The majority of the muscle cells were separated into fibril fragments. However rather short muscle cell parts which were surrounded by a more refractive connective tissue structure, exceeding in thickness the fibrils and resembling a spiral rim, could be seen. This structure, composed of circular fibres, was interrupted in many places, due to treatment in the homogenizer. As a matter of consequence, the originally presumably regular and dense 'winding' became not only loose but also the fibril bundles, freed from the elastic hold, were also — so to speak — escaping from the tight connective tissue grasp. As the loosened, here and there, ruptured circular fibres slipped towards one another, the fibril bundles appeared between them like a hernia.

Fig. 1 shows a relatively intact muscle cell. At one spot, however, the fibrils are already protruding under the connective tissue 'wire', holding together still concentrically and rather regularly. In Fig. 2 the 'winding' has been damaged more severely, and this phenomenon is still more apparent in Figs. 3 and 4.

In order to clarify the nature of the fibre structure holding together the muscle cells, the muscle tissue disintegrated in the homogenizer was held for 24 hr. at room temperature in 0·2 *N* sodium hydroxide solution, then, after washing in water, placed in hot 0·66 per cent solution of tartaric acid for 30 min. The purpose of this treatment was to remove the muscle protein and the collagen. Fig. 5 illustrates a preparation treated in such a way, on which the faint design of the fibre structure showing the outline of the muscle cell can be recognized. This test seems to verify the collagenous fibrous nature of the structure. This might be the exterior fibrous envelope surrounding the homogeneous membrane of true sarcolemma, as described by Wang.

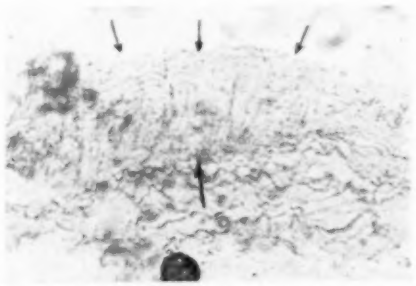

Fig. 5. A fragment of muscle fibre, treated in 0·2 *N* sodium hydroxide solution and then in hot 0·6 per cent tartaric acid solution (arrows). The concentric fibres have disappeared and only their traces can be detected. (× 250)

Fig. 5 presents some fine undulating elastic fibres which presumably belong to the endomysial connective tissue.

[1] Jones, W. M., and Barer, R., *Nature*, **161**, 1012 (1948).
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UBIQUINONE (COENZYME *Q*) AND THE FUNCTION OF VITAMIN E

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VITAMIN E comprises a small group of closely related substances, the most important of which is α-tocopherol. α-Tocopherol is widely distributed in the plant kingdom, has been found in unicellular organisms[1], yeasts and fungi[2], and, so far as we are aware, occurs in all animal tissues. It can be readily observed in even the most carefully prepared 'vitamin E-free' diets[3] based on natural foodstuffs and also in all the tissues of animals reared on such diets, provided that suitable analytical procedures are used. Although it appears likely that vitamin E is a normal constituent of most living things, little is known of its biochemical role, and nutritional vitamin E-deficiency in animals is characterized by a great variety of clinical, physiological and histopathological symptoms, the very diversity of which has usually proved more of an embarrassment than a help in attempts to understand the fundamental

processes involved in the deficiency state. Thus chicks may exhibit three different vitamin E-deficiency syndromes (muscular degeneration, exudative diathesis or encephalomalacia), separately or together, depending on the composition of their diet. Some species, such as the rat, are affected by failures in reproduction due to a variety of causes; other species, such as the pig, suffer hepatic disorders; still other species are subject to diseases chiefly affecting vascular or adipose tissue.

It is essential for an understanding of the role of vitamin E that these diverse manifestations produced by the same deficiency should be correlated with function, and we have already made the suggestion that animal tissues can suffer local and specific tocopherol deficiencies that may account for the nature of the syndrome in any given species[3,4].

A great advance was made, if not in our understanding, at least in our appreciation of the complexities of the vitamin E problem, when Schwarz and Foltz[5] discovered that selenium was able, like α-tocopherol, to prevent nutritional hepatic necrosis in the rat. Since then, many other workers have demonstrated that selenium and α-tocopherol have similar physiological effects in preventing some, but by no means all, of the symptoms of deficiency in a variety of animal species, and it is now certain that a fuller comprehension of the function of vitamin E must include an understanding of the role of selenium, both with regard to their similarities and even more to their interesting differences. It seems reasonably clear that at least three types of deficiency state can be discerned in animals: (1) diseases such as the hepatic necroses of the rat, mouse and pig, and the exudative diathesis of chicks, which can be prevented with either tocopherol or selenium, partially or totally; (2) at least some, and possibly all, disorders of reproduction and fertility (as in the rat, chick, and turkey) as well as encephalomalacia in the chick and muscular dystrophy in the rabbit, which can only be prevented with tocopherol; (3) muscular degenerations in species such as the sheep, which may be primarily due to selenium deficiency, although they can be either prevented or ameliorated by tocopherol. To these three conditions (and there are no doubt other intermediate states still to be elucidated) may perhaps be added a further category, namely, diseases of adipose tissue, such as the 'yellow fat' diseases of the cat and mink, in which only tocopherol appears to play a part. Formally the latter may fall within the realm of category (2) above, but because of the unusually clear effects on lipid metabolism in diseases affecting adipose tissue, they may with advantage be separated at present.

Active Metabolite of α-Tocopherol

In this article we wish to examine in further detail the nature of the function of α-tocopherol in animals and present some new evidence concerning its biochemical role. We have shown previously[3,4] that deficiencies of tocopherol and selenium in the rat and the rabbit produce a decrease in tissue levels of ubiquinone (coenzyme *Q*). It was also shown that dietary supplementation or oral dosage with either substance produced marked increases in ubiquinone concentrations in these animals (these effects can also be produced in avian species—to be discussed elsewhere), and we have already discussed[3] some possible connexions between these observations and the physiological effects of vitamin E in animals. In these earlier experiments our general technique was to give doses of α-tocopherol to deficient animals and kill them after 72 hr., after which time ubiquinone was measured in their tissues by methods described previously[6]. Table 1 gives the results of an experiment in which rats were given intravenous injections of 500 μgm. of α-tocopherol and examined after 2 hr. The technique in this and in similar experiments described afterwards was as follows: The animals in each test, randomized into appropriate groups, were anæsthetized lightly with ether. Tocopherol (emulsified in normal saline, containing 'Tween 80') was administered intrajugularly, and the wound was then closed with a clip and the animals allowed to recover. The operation generally took only a few minutes, and during the remainder of the experiment the rats behaved normally. At the end of the appropriate test period the rats were killed. Pilot experiments showed that ether anæsthesia had no effect on ubiquinone-levels, except after prolonged and heavy administration (and then, usually, only in the kidney). In the experiment summarized in Table 1, marked increases in the ubiquinone-levels of heart, liver and kidney were produced 2 hours after injection with tocopherol and, most significantly, the increase that occurred in heart was observed before any increase in the tocopherol concentration in this organ could be detected. (In the Tables, the symbols UQ, UC and T have been used to signify ubiquinone, ubichromenol and tocopherol, respectively.) In subsequent experiments (not shown) the latter phenomenon could sometimes be observed in other tissues, depending on the dose administered and how soon afterwards the animals were killed. As a result of these experiments, it seemed possible that the effect on ubiquinone was produced not by tocopherol but by a metabolite—perhaps a water-soluble derivative—formed from it. Such metabolites are in fact known. Simon *et al.*[7] isolated two water-soluble degradation products of α-tocopherol from the urine of rabbits that had been given large oral doses of the vitamin. These two substances were shown to be 2-(3-hydroxy-3-methyl-5-carboxy)-pentyl-3,5,6-trimethylbenzoquinone (I) and the lactone (II) derived from it. Although these workers seem to have regarded the compounds at that time as excretory products, Mertz and Schwarz[8] showed them to be highly active, *in vitro*, in preventing the respiratory failure that occurs in liver slices taken from rats deficient in tocopherol and selenium, and Corwin and Schwarz[9] have recently found them to be as active as tocopherol in maintaining α-ketoglutarate oxidation in tocopherol-deficient liver homogenates. We obtained a generous supply of lactone (II) from Dr. J. Weichet of Prague

Table 1. Effect of α-Tocopherol administered intrajugularly to Rats

Group and treatment	Heart			Liver			Kidney		
	UQ	UC	T	UQ	UC	T	UQ	UC	T
Controls	128	7	1·7	63	15	0·9	49	3	1·9
2 hr. after injection of α-tocopherol (500 μgm.)	166	8	1·5	74	22	13·7	88	9	5·2

Two groups of six male rats, 4 months old, on diet *E10Y*. Results are in μgm./gm. of fresh tissue

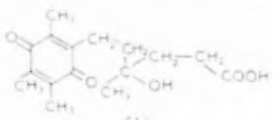
Table 2. Effect of Tocopheronolactone given orally and intravenously to Rats

Group and treatment	Heart UQ	Heart UC	Heart T	Liver UQ	Liver UC	Liver T	Kidney UQ	Kidney UC	Kidney T
Controls	94	7	1·0	32	12	1·0	69	2	1·1
24 hr. after 1 mgm. tocopheronolactone orally	134	8	1·0	33	12	1·2	101	4	1·1
15 min. after 25 μgm. tocopheronolactone intravenously	166	18	1·3	50	19	1·0	81	4	1·3

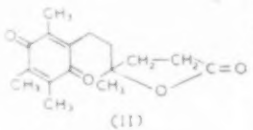
Three groups of six male rats, 9 months old, on diet *E*10Y. Results in μgm./gm. of tissue

(and later synthesized it in our laboratories) and examined it for its effect on ubiquinone in a number of experiments, some of which are summarized in Table 2.

It was found to be highly active, even more so than α-tocopherol itself when given in an equimolecular amount, either orally or when given intravenously. Marked increases in ubiquinone could be produced *within* 15 *min.* of injecting as little as 25 μgm. of lactone (II) intravenously into fully grown rats. In view of the likely physiological significance of these two metabolites, therefore, we propose that the name tocopheronic acid be given to compound (I) and that compound (II) be called tocopheronolactone.

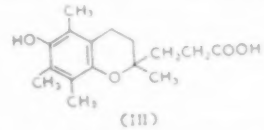


(I)



(II)

We have shown previously[10] that whereas α-tocopherol or selenium can control ubiquinone-levels in most tissues of the rat, only tocopherol is effective in the uterus, a phenomenon that is probably connected with the inability of selenium to prevent gestation-resorption. Since such important differences between tissues exist, it was clearly important to discover whether tocopheronolactone was as effective as α-tocopherol in the uterus and (for allied reasons) in the ovary. Table 3 gives the results of an experiment in which female rats were given oral doses of (*a*) sodium selenite, (*b*) α-tocopheryl acetate, or (*c*) tocopheronolactone, and killed 24 hr. later. Heart, ovary and uterus were analysed. Tocopheronolactone was found to be as active as α-tocopherol in all three tissues, and the experiment again confirmed the inactivity of selenium in uterus. Finally, Table 4 gives the results of an experiment that illustrates the differences in the rates of action of α-tocopherol and its metabolite. Rats were injected intrajugularly with small amounts of each substance (in equimolecular amounts). Groups of rats were killed both after 15 min. and after 120 min. and three tissues were examined in the usual way for effects on ubiquinone and ubichromenol. These were compared with tissues from negative and uninjected controls and also from groups of rats injected with bland saline 'Tween 80' solutions (used as vehicles for the tocopherol and tocopheronolactone). The results show that whereas after 15 min. the tocopherol was just beginning to take effect, the lactone was already fully active at this time in kidney and nearly so in heart and liver. After 2 hr. the effect of tocopherol was maximal, whereas the effect of tocopheronolactone in kidney was already on the wane, although it was still pronounced in heart and liver. An interesting feature of the analyses is that 150 μgm. of tocopherol was obviously insufficient to produce appreciable changes in the tocopherol-levels of the tissues: this quantity given to deficient animals can clearly be rapidly and practically completely metabolized during the 2-hr. period. In this experiment we also studied the effect of the interesting chromanol (III) (also prepared



(III)

by Dr. Weichet), which is derived from tocopheronic acid. Although this substance was active in increasing ubiquinone in heart, it was quite ineffective in liver and kidney, where, indeed, ubiquinone-levels were actually depressed. These four experiments suggest that tocopheronic acid is either the physiologically active agent produced from tocopherol or that it is closely allied to such a derivative. We have had some indication that tocopheronolactone may itself be converted to another substance *in vivo*. Chromatograms of tissue extracts from rats given fairly large amounts of the lactone (1–2 mgm.) have shown the presence of a non-reducing lipid-soluble substance, chromatographically slower than α-tocopherylquinone in reversed-phase systems and therefore possibly of greater molecular weight, which spectroscopically appeared to be a typical

Table 3. Effect of α-Tocopherol, Tocopheronolactone and Selenium in Rat Heart, Ovary and Uterus

Group and treatment	Heart UQ	Heart T	Ovary UQ	Ovary T	Uterus UQ	Uterus T
Controls	30	0·5	48	18·4	33	0·8
Selenite	57	1·1	76	16·8	37	2·4
Tocopherol	131	4·5	88	61·0	50	6·9
Tocopheronolactone	118	0·6	96	16·5	48	3·2

Groups of nine female rats (5 months old on diet *E*10Y) were used. Rats in test groups were given (*a*) 40 μgm. sodium selenite, or (*b*) 10 mgm. α-tocopheryl acetate, or (*c*) 2 mgm. tocopheronolactone, and killed 24 hr. later. Results are in μgm./gm. of tissue

Table 4. Comparison of Effects of α-Tocopherol and Tocopheronolactone

Group and treatment	Time after injection (min.)	Heart UQ	Heart UC	Heart T	Liver UQ	Liver UC	Liver T	Kidney UQ	Kidney UC	Kidney T
No injection	0	32	9	1·1	25	16	0·4	56	25	8·4
Bland injection	15	33	9	1·2	26	20	0·4	52	20	6·6
Bland injection	120	36	9	1·3	25	18	0·5	60	22	6·9
α-Tocopherol	15	47	5	1·7	42	21	1·8	50	9	9·5
α-Tocopherol	120	85	N.D.*	1·4	58	27	1·7	88	7	9·2
Tocopheronolactone	15	72	1	1·5	38	19	0·4	86	5	6·8
Tocopheronolactone	120	145	N.D.*	1·8	51	27	0·4	56	2	8·2
Chromanol (III)	30	137	N.D.*	1·8	18	11	0·5	50	19	2·8

Male rats (5 months old, on diet *E*10Y) were injected intrajugularly with α-tocopherol (150 μgm.) or tocopheronolactone (100 μgm.) or chromanol III (100 μgm.) dissolved or suspended in saline 'Tween 80' solution. Control rats were used with and without injections of bland saline/'Tween 80' solutions as two types of negative control. Results in μgm./gm. of tissue

* N.D., not detected.

substituted benzoquinone ($\lambda_{max.}$ at 259 and 268 mμ.), reducible with borohydride. Its significance is at present quite unknown.

Factors affecting Ubiquinone-levels in the Rat

It has become apparent from work with many groups of rats that tissue ubiquinone-levels in this species are subject to marked fluctuation, particularly in vitamin E-deficient animals but also in normal rats from the stock colony. Although the factors responsible are in the main unknown at present, one such factor is undoubtedly the nature of the diet, especially with regard to traces of vitamin E and selenium, but also with regard to gross composition. The diet (*E10Y*) used in our experiments contained very little tocopherol. Its composition was as follows: dried yeast (Marmite Food Extract Co.), 25; casein ('Genatosan', low vitamin content), 10 per cent; lard, 1 per cent; sucrose, 59 per cent; McCollum's salt mixture, 5 per cent; with the addition of 10 I.U. of vitamin A and 2·5 I.U. of vitamin D/gm. of diet. We have found that the use of this diet consistently produces low ubiquinone-levels in the rat, especially in liver. This can be seen from the results (Table 5) of an experiment that deals with another factor having a marked effect on ubiquinone-levels, namely, starvation. In this experiment, groups of rats on 3 diets were examined, in comparison with the controls, after being fasted for 18 hr. One group was fed diet *E10Y* for 6 months, the second group received the same diet supplemented with 100 mgm./kgm. of α-tocopheryl acetate, and the third group was on the adequate stock colony diet. Starvation increased ubiquinone markedly in the stock colony animals, less so in the other groups, but significantly in all livers. These observations are of especial interest since cholesterol synthesis is known to be markedly depressed in liver during fasting, and both the ubiquinone side-chain and cholesterol are derived from a common precursor, mevalonate. Bucher[11] has discussed some of the factors that might be concerned with the inhibition of cholesterol synthesis in fasted animals. Although these are far from clear, it appears that the process leads to a concurrent increase in ubiquinone (the amount of the latter in tissues being, of course, fairly small compared with the amounts of cholesterol). It should be noted that other factors have also been found to increase ubiquinone in the rat: these include uncoupling agents such as thyroxine and dinitrophenol[12] and substances that inhibit oxidation without uncoupling of phosphorylation[13], such as barbiturates (fuller details of this work will be presented elsewhere). In spite of the multiplicity of these effects, the possibility that they influence some common point in metabolism, of which the increase in ubiquinone may be only one aspect, must be considered.

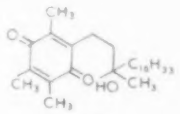
Table 5. Effect of Starvation on Ubiquinone-9 and Ubichromenol-Levels in Vitamin E-deficient and Adequately Fed Rats

Group	Treatment	Heart UQ	Heart UC	Heart T	Liver UQ	Liver UC	Liver T
E-deficient	Non-fasted	37	15	1·8	15	11	0·4
	Fasted	38	15	1·8	23	5	0·4
E-def. + E	Non-fasted	58	8	6·2	28	13	10·5
	Fasted	60	4	5·0	34	8	5·0
Stock diet	Non-fasted	39	N.D.*	3·3	83	23	11·5
	Fasted	66	N.D.*	9·8	121	37	9·1

For details of diets, see text. Results in μgm./gm. of tissue.
* N.D., not detected.

α-Tocopherylquinone

The discovery of physiological activity for tocopheronolactone inevitably raises anew the problem of α-tocopherylquinone. This substance (IV), the irreversible oxidation product of α-tocopherol, is only present in traces in animal tissues (see Diplock *et al.*[10]).



(IV)

Many workers, searching for evidence of a reversible oxidation-reduction reaction of α-tocopherol in tissues, have examined this quinone for activity of vitamin E and reported it to be inactive[14]. However, there seems superficially to be no obvious reason why it should not be as easily degradable to tocopheronolactone as α-tocopherol itself, and if this is so it also should be effective in increasing ubiquinone-levels. Accordingly, we prepared a specimen of α-tocopherylquinone and purified it until it was rigorously freed from any traces of reducing material and was chromatographically homogeneous. When it was given orally to vitamin E-deficient rats (10 mgm. to each animal), it increased ubiquinone-levels markedly, in the same way as tocopherol. Moreover, analysis of the tissues showed conclusively that no conversion to tocopherol had occurred, nor could the presence of tocopherylquinone itself be detected.

It seemed therefore that the reason for the lack of vitamin E activity of α-tocopherylquinone might reside in the inability of the animal to store or transport it. In order to study this possibility, the quinone was examined in a rat gestation-resorption assay test in the following manner. Virgin female vitamin E-deficient rats (4–5 months old) were mated and given 5 mgm. of the quinone (dissolved in propylene glycol/10 per cent ethanol) intraperitoneally and 5 mgm. of the quinone orally (in 'Tween 80' emulsion) every day between the 7th and 13th days of pregnancy. This dosage was completely effective in preventing fœtal resorption, proving that tocopherylquinone has vitamin E activity if given in adequate amounts to rats during gestation. We have recently become aware of the demonstration by Mackenzie and Mackenzie[15], using virtually identical methods, of the vitamin E activity of tocopherylhydroquinone, which these workers predicted by a process of reasoning quite different from ours. Their belief, however, that there is an essential difference between the quinone and the hydroquinone would now appear to be invalid: any quantitative discrepancies between the activity of quinone and hydroquinone can probably be explained by differences in the absorption and transport of the two substances. As a matter of history, the discovery of vitamin E activity for the quinone confirms the prognostication of Smith, Renfrow and Opie[16] made in 1942, when they found high biological activity for α-tocopheramine (which gives the quinone on oxidation). We have tried, so far without success, to demonstrate comparable activity for either tocopheronolactone or chromanol (III)

(given intraperitoneally at 4 and 3 mgm. day respectively from the 7th to the 13th day of pregnancy) in the rat gestation-resorption test. In view of the solubility characteristics of the former and the rate at which it seems to be excreted, maintenance of adequate levels throughout the gestation period might be expected to be difficult and such levels may not have been attained with the small quantities of the lactone at present available to us.

Vitamin E and Lipid Peroxidation

It is now possible to discuss, in somewhat better perspective, the important question of the relation between the total biological function of vitamin E and its role as a lipid antioxidant. It has been the view of many workers that in fact the two functions are identical, but we believe that this view can no longer be accepted. We have shown previously[16,17] that the effect of tocopherol and selenium on ubiquinone is probably independent of any antioxidant role that vitamin E might have, and this is now further supported by the finding that tocopheronolactone is likely to be the active vitamin E metabolite controlling ubiquinone-levels. There is, of course, much nutritional and physiological evidence that undoubtedly suggests that α-tocopherol does play an important part in fat metabolism, protecting oxidizable lipids from destruction and perhaps preventing the accumulation of potentially toxic compounds in tissues. It seems reasonable to accept that α-tocopherol functions as a conventional lipid antioxidant, for at least some of its physiological effects can be duplicated by non-physiological antioxidants. However, in recent years, partly because of the many and persistent failures to demonstrate a more specific role for α-tocopherol in animals, it has proved tempting to explain the total role of vitamin E in terms of its antioxidant properties and to suggest that all the nutritional requirements for vitamin E can be satisfied by a physiological lipid antioxidant.

It is this hypothesis that we now wish to examine in some detail. Much of the evidence on which it is based stems from the demonstration that respiring mitochondrial preparations[18,19] and whole homogenates[20] exhibit a phenomenon usually referred to as 'lipid peroxidation' and that this can be inhibited by the *in vitro* addition of α-tocopherol, antioxidants, or certain metallic ions such as those of cobalt and manganese. Dietary supplementation with tocopherol has been shown, in a few instances, to reduce tissue peroxidation; and certain characteristic symptoms of vitamin E deficiency, such as rat erythrocyte haemolysis[21] and impairment of ascorbic acid synthesis in rat liver[22] are always accompanied by an increase in peroxidation, and both are reversed *in vitro* by α-tocopherol. Lipid peroxidation itself appears to be poorly understood and is obviously a simple term for a complex process. *In vivo* peroxides and *in vitro* peroxidation (the latter after incubation of tissue preparations at 37° for periods varying between 15 min. and 1 hr.) are usually determined by adding thiobarbituric acid (TBA) and measuring the red colour produced. It is usually considered that the TBA-reacting substance is malonaldehyde[23]. The *in vitro* peroxidation is considered to be a 'development' of a process that has already produced changes in the tissues, and it is known to be greatly enhanced by the presence of ascorbic acid, which catalyses many peroxidations. Kitabchi *et al.*[22] have shown that peroxidation in tissues is mainly microsomal in origin, the malonaldehyde being produced by a reaction between a microsomal lipid and a metal ion or an intermediate formed from gulonolactone or ascorbic acid. They suggest that peroxidation is closely related to the impairment of ascorbic acid synthesis that occurs in vitamin E deficiency.

We have already discussed certain aspects of the antioxidant theory[5] and have shown that study of the tocopherol concentrations in different tissues leads to the conclusion that there is no real relationship between these concentrations and the extent of lipid peroxidation. For example, the rat adrenal contains several times as much tocopherol as any other tissue in the body and yet peroxidizes very easily[24]. Moreover, in most tissues of the rabbit[18] and also in the rat[21], there are no significant differences between the *in vivo* peroxides of vitamin E-deficient and adequately fed animals. It has been suggested[19] that the TBA reactants found in the tissues of adequate animals do not represent lipid peroxidation products; but this appears to involve a circuitous argument, and, as we show below, they are in fact indistinguishable from the 'peroxides' of deficient animals. It is agreed by all workers who have investigated the phenomenon that whereas *in vitro* lipid peroxidation can easily be prevented in liver and perhaps muscle by the addition of tocopherol to deficient diets, such an effect cannot be obtained in other tissues. For example, Carpenter *et al.*[20] found that rat testis, a tissue particularly susceptible to the effects of vitamin E deficiency, synthesized peroxides *in vitro*, even when taken from animals given sufficient tocopherol to prevent deficiency. Bieri and Anderson[25] had to feed relatively huge amounts of tocopherol for long periods to prevent lipid peroxidation in rat testis and even then they were unable to effect any appreciable reduction in brain and kidney.

Table 6 summarizes the results of an experiment in which we have studied lipid peroxidation in pregnant female rats from the stock breeding colony and similar rats from the vitamin E-deficient colony. Both groups were mated and pregnancies allowed to continue to the 18th day: this is the time at which rats are normally examined in the standard rat gestation-resorption assay for vitamin E and resorbed

Table 6. Lipid Peroxidation in Stock Colony and Vitamin E Deficient Pregnant Rats

Group	Test	Liver	Uterus*	Foetus	Placenta
Stock colony	*In vivo* peroxides	6 (2)	3 (5)	4 (5)	4 (2)
	In vitro peroxidation†	12 (5)	5 (5)	10 (3)	5 (2)
	In vitro + ascorbate‡	12 (5)	5 (7)	19 (4)§	5 (2)
				(Total uterine contents)	
E-deficient	*In vivo* peroxides	10 (13)	4 (4)	5 (4)	
	In vitro peroxidation†	22 (5)	9 (3)	7 (1)	
	In vitro + ascorbate‡	34 (12)	17 (6)	22 (4)	

Results are given as direct readings of the optical density at 520 mμ after reaction of 4 ml. of a 2 per cent homogenate with TBA. Each result is a mean followed by number of rats separately tested.

* This tissue could not be homogenized and was used as a fine suspended mince.

† Incubation time of 15 min. for liver, 60 min. for other tissues.

‡ 3×10^{-4} mole of ascorbic acid added before incubation.

§ One discordant result was found in another rat in this group.

fœtuses counted. The rats were killed and liver, uterus, placenta and live fœtuses taken from the stock animals, and liver, uterus and total uterine contents (combined resorbing fœtuses and placentæ) from the deficient group. Individual tissues from each animal were examined for *in vivo* peroxides and *in vitro* lipid peroxidation by methods described in detail elsewhere[21-25]. In all the tissues of the deficient animals, peroxidation increased after *in vitro* incubation, particularly in the presence of ascorbate. In the adequate animals, however, although peroxidation was low in liver, uterus and placenta, the viable fœtuses peroxidized almost as much as the total resorbed uterine contents of the vitamin E-deficient group. It is especially significant that this fœtal peroxidation in the adequate tissues increased in the presence of ascorbic acid (compare liver and uterus, where it did not), suggesting quite strongly that the phenomenon is identical with the 'lipid peroxidation' of deficient tissues. The significance of this experiment is that the viable 18th-day rat fœtus, *by classical definition*, contains sufficient vitamin E for all its needs and the conclusion must be that, at least in this instance, the TBA reaction cannot bear any relation to vitamin E function.

It would in fact appear from the series of experiments now to be described that even the 'inhibition' of lipid peroxidation may not prove to be explicable solely in terms of the reducing or antioxidant properties of α-tocopherol itself. In these experiments, the results of which are given in Table 7, a number of substances were examined for their activity in preventing the *in vitro* peroxidation of vitamin E-deficient rat liver homogenates. The substances tested clearly fall into two groups: (1) those as active as α-tocopherol, which include only thyroxine and, most remarkably, the non-reducing substance, tocopheronolactone, and (2) those with only about one-tenth of the activity of tocopherol, which comprise the ubiquinones, ubichromenol, α-tocopherylquinone, the quinone reduction products (quinols), vitamin A, and menadione. The quinols were obtained from the corresponding quinones by reduction in ethanol with aqueous potassium borohydride and maintained in the reduced state with an excess of reagent (pilot tests showed that borohydride had no significant effect in preventing peroxidation).

Table 7. Effect of α-Tocopherol, Tocopheronolactone and some Quinones on Inhibition of *in vitro* Lipid Peroxidation in Liver Homogenates

	Per cent reduction in peroxidation (TBA test)	Amount of active substance used (moles)
α-Tocopherol	94	5×10^{-7}
	c. 50	2.4×10^{-6}
Substances as active as α-tocopherol		
L-Thyroxine sodium salt	93	5×10^{-7}
	c. 50	2×10^{-6}
Tocopheronolactone	79	1×10^{-6}
	c. 50	2×10^{-6}
	36	1×10^{-5}
Reduced tocopheronolactone (quinol)	25	1×10^{-6}
Substances with about one-tenth or less of the molar activity of α-tocopherol		
α-Tocopherylquinone	40	2×10^{-7}
	9	2×10^{-6}
α-Tocopherylhydroquinone	25	2×10^{-6}
Ubichromenol 50	32	2×10^{-7}
Ubiquinone 30	20	4×10^{-7}
Ubiquinone 35	31	4×10^{-7}
Ubiquinone 40	23	4×10^{-7}
Ubiquinone 45	13	4×10^{-7}
Ubiquinone 50	19	4×10^{-7}
Ubiquinol 45	0	4×10^{-7}
Ubiquinol 50	8	4×10^{-7}
Menadione	76	5×10^{-7}
Vitamin A alcohol	44	2×10^{-7}
Vitamin A palmitate	81	1×10^{-6}
Vitamin K_1	56	1×10^{-7}

The results show that conversion of the quinones to quinols only enhances the activity very little. This may be because the quinones are, in any event, mainly reduced to quinols under the conditions of test; ubiquinone can be reduced by many substrates[27], and both menadione[28] and tocopheronolactone[29] can be enzymatically reduced by diphosphopyridine nucleotide. The evidence, however, is not incompatible with the assumption that the non-reducing quinones themselves may participate in the inhibition of 'lipid peroxidation'. For example, it has not so far proved possible to demonstrate that tocopherylquinone can be reduced either *in vivo* or by *in vitro* biochemical systems[30,31]. It was considered as a possibility that the activity of tocopherylquinone could be accounted for by an enzymatic cleavage to tocopheronolactone under the conditions of incubation; however, when tocopherylquinone was pre-incubated for 60 min. with a liver homogenate and then re-tested for its effect on peroxidation in a fresh homogenate, only a small enhancement of activity could be demonstrated.

Another interesting observation from Table 6 is that vitamin A has 'antioxidant' activity, as measured by the 'lipid peroxidation' test, although it is a substance that can scarcely be considered as a conventional antioxidant: it is difficult to see why the addition of an unsaturated lipid like vitamin A should protect against peroxidation (although we have observed similar effects at a higher concentration with substances such as nerolidol, farnesol and geranyllinalool).

Since vitamin A is an important constituent of liver, which has not only been extensively used for studies of peroxidation but also provides a good deal of the evidence for the effect of vitamin E, it seemed important to examine its influence on 'lipid peroxidation' in this tissue. Three groups of male rats were placed, at the age of 21 days, on a diet deficient in both vitamin E and vitamin A. After a month, one group was transferred to the same diet supplemented with 10 I.U. of vitamin A/gm., the second group to the same diet supplemented with 40 I.U. of vitamin A/gm., and the third group remained as vitamins A- and E-deficient controls. After a month on these diets, the rats were killed and livers and brains pooled for studies of their 'lipid peroxidation'. As Table 8 shows, there was indeed a marked 'antioxidant' effect in both tissues containing vitamin A: this is doubly remarkable since, as we show elsewhere[26], the *vitamin E* concentration in liver deficient in vitamins A and E may be several times higher than in control livers deficient only in vitamin E (because of the well-established antagonistic effect of vitamin A on tocopherol). The same is true of brain; and, in fact, in this tissue the 'antioxidant' effect of dietary vitamin A is at least as great as we have ever obtained with dietary vitamin E (see also Bieri and Anderson[32]). It can be concluded, therefore, that vitamin A must also be considered as a factor in reducing 'lipid peroxidation' as measured by the TBA test, particularly since the addition of tocopherol to homogenates protects vitamin A from destruction.

Table 8. Effect of Dietary Vitamin A on 'Lipid Peroxidation' of Rat Liver and Brain

	Peroxides† (E at 520 mμ) Liver‡			Brain‡		
Level of dietary A, I.U./gm.	0	10	40	0	10	40
In vivo test	4	2	2	2	1	1
Incubated at 37°	17	21	13	42	37	28
Incubated with ascorbate*	51	38	27	118	120	91

* 3×10^{-4} mole of ascorbic acid in 4 ml. of homogenate.
† Each result is a mean of two determinations.
‡ Liver incubated for 15 min., brain for 60 min.
For details of diets, see text. Results are given as direct readings at 520 mμ of the TBA reaction.

The picture of 'lipid peroxidation' is still further complicated by considerations of another series of experiments (summarized in Table 9), in which tocopheronolactone and tocopherylquinone were examined for their activity in preventing erythrocyte hæmolysis in rats. This hæmolysis, which is produced by incubation with dialuric acid, is an early and characteristic symptom of vitamin E deficiency in the rat[32] and can be completely reversed if the cells are pre-incubated *in vitro* with α-tocopherol or if the animal is given vitamin E orally some time before the blood is taken. Many other substances, some of them non-reducing, can also inhibit hæmolysis[33] and this inhibition is always accompanied by a decrease in the lipid peroxidation (thiobarbituric acid reaction) of the erythrocytes[21]. As Table 9 shows, tocopheronolactone and tocopherylquinone were both negligibly active when given orally; but the latter substance, in strong contrast to the former, was found to be quite active *in vitro* both in inhibiting hæmolysis and in reducing peroxidation. Now, lipid solubility *per se* is not a factor that determines the *in vitro* activity of substances in the hæmolysis test: we have shown[32], for example, that ubiquinone 50 is inactive, whereas thyroxine affords complete protection[21]. It is, moreover, unlikely (judging from the results in Table 7) that tocopherylquinone is more easily reduced to a quinol on the surface of the erythrocyte than tocopheronolactone would be. While these results are not easy to interpret, they provide still further evidence that the relation between the effect of antioxidants and 'lipid peroxidation' on one hand and between 'lipid peroxidation' and the thiobarbituric acid reaction on the other needs to be reconsidered.

Table 9. Effect of Tocopheronolactone and α-Tocopherylquinone on Rat Erythrocyte Hæmolysis, *in vivo* and *in vitro*

Substance	*In vivo* potency (D-α-tocopheryl acetate = 100)	*In vitro* potency (DL-α-tocopherol = 100)	Protection, *in vitro* against peroxidation
Tocopheronolactone	< 10 (if any)	< 1 (if any)	Nil
Tocopherylquinone	< 3 (if any)	*c.* 10	complete
Tocopherylhydroquinone	< 3 (if any)	—	—

Possible Functions of Vitamin E

Although it is still difficult to present a unified concept that will explain satisfactorily the role of vitamin E in animals, several developments in the past two or three years signify a new approach to the problem that will certainly prove to be most productive. In our opinion, the present position may be summarized as follows: Vitamin E must have at least two functions, which at present have to be considered independently, but which may prove to be closely related. One is concerned with the metabolism of unsaturated lipids, in which role its antioxidant properties probably play a part: however, the connexions between this function and the phenomenon that occurs in tissues and is termed 'lipid peroxidation' seems to us, for many reasons, still to be obscure and may yet prove to be an example of a biochemical truism. It is perhaps not altogether surprising that this should be so. It is only necessary to examine the findings by Carpenter *et al.*[20] and Kitabchi *et al.*[22] on the relation between tocopherol and ascorbic acid synthesis to appreciate the subtleties that might be involved in the TBA reaction. Thus, tocopherol increases the synthesis of ascorbic acid, which itself catalyses fatty-acid peroxidation and inhibits its own synthesis[22]: tocopherol inhibits malonaldehyde production, but ascorbic acid increases it markedly[22]: and, contrarily, ascorbic acid enters into a potent synergistic relationship with tocopherol in preventing the hæmatin-catalysed peroxidation of unsaturated fatty acids[24]: the possibilities of feedback mechanisms are obviously many and intricate.

The second function of vitamin E, in which the active substance is almost certainly a metabolite of α-tocopherol, possibly tocopheronolactone, results in the biogenesis of ubiquinone. Two key questions immediately present themselves: How far is it possible to understand the physiological and histopathological symptoms of vitamin E deficiency (with the exception of those relating in the narrow sense to lipid antioxidant effects) in terms of ubiquinone deficiency? Is the effect of tocopherol on ubiquinone a unique effect on its synthesis or only a secondary phenomenon resulting from a more fundamental process elsewhere? Although answers to these questions must await further work, it is reasonable even now to suggest that at least some of the disturbances in respiration, oxidation, and tissue (particularly embryonic) differentiation in vitamin E deficiency states may be explicable in terms of the effect on ubiquinone-levels. In the rat, and probably in other species, there is an alternate mechanism, involving selenium, which also influences biosynthesis of ubiquinone. The two mechanisms appear to be parallel, since in most tissues of the adult rat, as shown elsewhere[25], tocopherol does not increase ubiquinone-levels if sufficient selenium is present and *vice versa*. In two organs, however, the two mechanisms are plainly of unequal importance. In uterus, the selenium-dependent process does not appear to be present at all, whereas in liver, where selenium exerts a remarkable influence on ubiquinone compared to that of tocopherol[2,10,25], the selenium-dependent mechanism is apparently preponderant. Such a difference between the effects of selenium and tocopherol is also found in the livers of avian species (to be discussed in a separate communication).

The existence of such alternate biochemical systems and the possibility that they may be of unequal significance in different tissues might account for the observed differences between the physiological effects of selenium and tocopherol in animals. It is at this stage not possible to say whether all animals require a supply of both tocopherol and selenium. The answer to this question may not only vary from species to species but also may differ at different periods during the life-cycle. Thus the

rat needs tocopherol specifically for reproduction (and perhaps during very early life), but during adult life its needs could conceivably be met by selenium. According to Nesheim and Scott[35] the chick has an absolute requirement for selenium even if tocopherol is supplied, and a similar position may exist in the lamb. Both Draper *et al.*[36] and, more recently, Crider *et al.*[37] have concluded that the rat does not need tocopherol if certain antioxidants are provided in the diet and that substances such as DPPD (N,N′-diphenyl-*p*-phenylene diamine) and ethoxyquin (1,2-dihydro-6-ethoxy-2,2,4-trimethylquinoline) can prevent reproduction failure in the rat.

We have analysed lard-casein diets identical in composition with those used by these workers, however, and have found them to contain enough tocopherol to supply about 40–70 μgm. per week to each rat. These amounts cannot be considered insignificant. Furthermore, as we have demonstrated elsewhere[38], ethoxyquin added to these so-called 'vitamin E-free' diets (especially those containing considerable amounts of vitamin A[26,27]) effectively spares tocopherol in rat uterus and in fact raises it to levels not incommensurate with it having some biological activity. Bieri *et al.*[39] have likewise suggested that the chick does not need tocopherol; but we have found that the diets used by these workers also contain appreciable amounts of tocopherol and that animals fed on them show significant tissue concentrations (to be published). There is no doubt that many of the discrepancies in these investigations—as well as the continued use of diets incorrectly believed to be free of vitamin E—stem largely from the use of inadequate analytical methods: only the more recently developed chromatographic procedures can deal satisfactorily with the small quantities of tocopherol relevant to investigations of vitamin E-deficient animals. It would seem that, if the absolute requirement of both the rat and the chick for α-tocopherol is to be determined, there is no alternative to the use of wholly synthetic diets. (In this connexion, even the methyl linoleate urea complex (Hormel Foundation), used by Crider *et al.*, has been found to contain about 3 μgm./gm. of α-tocopherol (and, in addition about 5 μgm./gm. of ubiquinone) which amounts are consistent with its method of preparation. The concentrate used by Draper *et al.* may have contained similar quantities. These figures illustrate some of the difficulties in work on vitamin E.)

Returning once more to the biochemical function of tocopherol, two points of interest need to be mentioned. First, is there any connexion between tocopherol and cholesterol synthesis? This much-neglected topic presents itself afresh in view of the contrasting effects of fasting on ubiquinone-levels and cholesterol synthesis, already referred to. There is already an area of confusion here: many workers[39,40] have shown that tocopherol has a marked hypocholesteræmic effect in the rabbit, but other workers[41] could not demonstrate this in the rat, whereas the results of Gray *et al.*[42] suggest that tocopherol might increase cholesterol synthesis in the rat. Secondly, is it possible to correlate the effect of vitamin E on ubiquinone with the demonstration by Corwin and Schwarz[9] that the decline in the oxidation of α-ketoglutarate by vitamin E-deficient liver homogenates can be prevented by *in vitro* addition of α-tocopherol, tocopheronolactone or menadione? Neither vitamin K deficiency nor menadione supplementation affects ubiquinone-levels in the rat (unpublished observations; see also Morton and Phillips[43]) and, furthermore, Corwin and Schwarz found dietary selenium to be inactive in restoring oxidation. It is possible, therefore, that although the effect of dietary selenium and tocopherol on hepatic necrosis may be related to their common role in ubiquinone biogenesis or processes leading to it, the effect of tocopherol in restoring respiratory decline in slices and of the ketoglutarate system may be due to yet another function of tocopheronolactone.

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PHOTOCHEMICAL SYNTHESIS OF AMINO-ACIDS AND A NEW TRANSAMINATION PROCESS BY TRANSFER OF FREE AMINO-RADICALS

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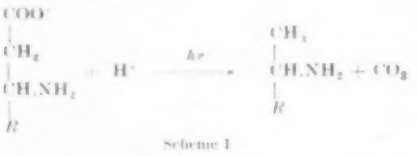
RECENT investigations conducted in our Institute[1,2] have shown that it is possible to synthesize amino-acids by ultra-violet irradiation of solutions containing a ternary organic compound together with a nitrogen compound, such as potassium nitrate, sodium nitrite, hydroxylamine and ammonium hydroxide. All the various steps of the photochemical process have been elucidated; the action mechanism of each of them has been established exactly, and a rational, co-ordinated interpretation has been deduced.

For reasons of brevity we report in Table 1 only a few examples of the syntheses accomplished by us.

Further investigations, which will be published in full in *Gazzetta Chimica Italiana*, have given results which we regard as interesting.

Amino-acids in acidified aqueous solution, when exposed to ultra-violet rays, undergo various changes, above all (scheme 1):

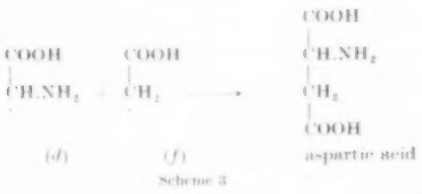
(1) Decarboxylation:



Scheme 1

(2) Radical decomposition by homolytic degradation, for example, scheme 2:

(3) Recombination of radicals, with formation of new amino-acids: the free radicals may recombine in the most varied ways, for example, scheme 3:



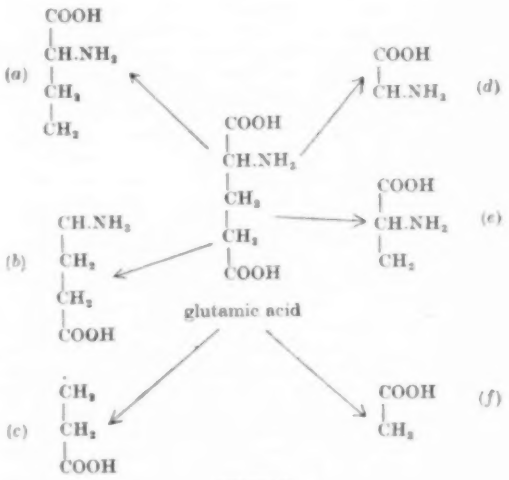
Scheme 3

Thus the radicals containing the amino-group may become 'transamination agents', in that they can determine the transfer of properties of the amino-group from one amino-acid to another of different molecular structure.

If the solution containing the amino-acid is irradiated in the presence of a properly chosen organic compound, capable, in its turn, of yielding free radicals, it is possible to direct the transamination process toward the formation of determinate synthesis products.

Table 1

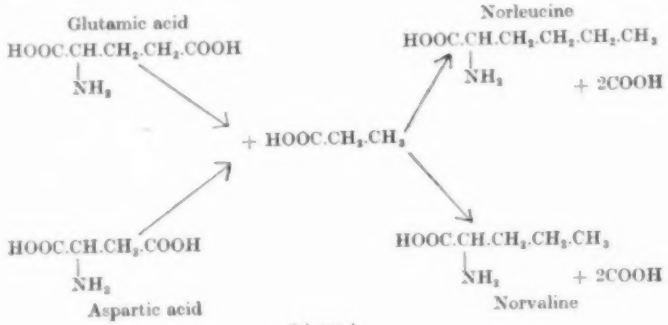
Organic substance irradiated with ultra-violet rays	Nitrogen compound present in the solution	Amino-acids obtained
Glutaric acid	KNO_2, KNO_3, NH_4OH	Glutamic acid, glycine, β-alanine, γ-amino-butyric acid, aspartic acid
Citric acid	KNO_2, KNO_3, NH_4OH	Glycine, β-alanine, serine, aspartic acid, γ-aminobutyric acid
Glucose	KNO_2, KNO_3, NH_4OH	Serine, glycine, aspartic acid



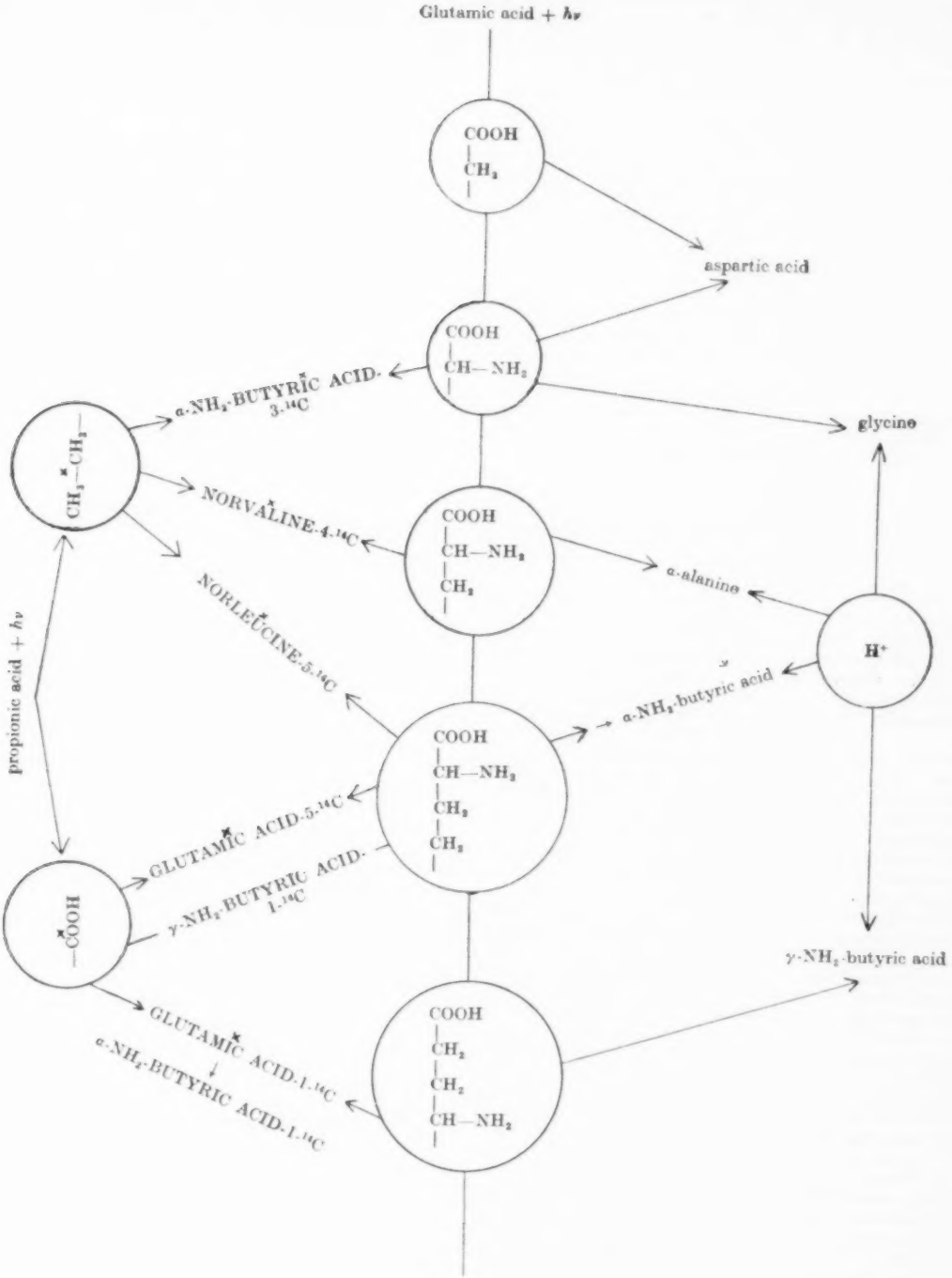
Scheme 2

For example, we have synthesized norleucine by irradiating glutamic acid in the presence of propionic acid, and have synthesized norvaline by irradiating aspartic acid in the presence of propionic acid.

The scheme of the reactions involved is shown in scheme 4:



Scheme 4



Scheme 5

Capital letters, radioactive compounds; small letters, non-radioactive compounds. *, radioactivity from propionic acid-1-¹⁴C; ×, radioactivity from propionic acid-2-¹⁴C.

(As has been experimentally established, the two —COOH radicals form oxalic acid.)

In order to demonstrate the mechanism of the process described we have employed both the chromatographic detection of the synthesized compounds and the isotopic tracer method. For the latter purpose we have used two types of propionic acid labelled with carbon-14 in positions 1 and 2, respectively ($CH_3.CH_2.COOH$ and $CH_3.CH_2.COOH$).

In all cases we have obtained a variety of amino-acids; but the examination of the autoradiographs obtained from the chromatograms has shown that the major part of the radioactivity is concentrated in the norvaline coming from aspartic acid and propionic acid-2-^{14}C, while the norvaline coming from propionic acid-1-^{14}C is completely inactive. Similar results have been obtained with the norleucine coming from glutamic acid + propionic acid. We have therefore succeeded in demonstrating the effect we sought.

We report the recombination scheme for the radicals obtained by exposing to ultra-violet rays the solution of glutamic acid + propionic acid-1-^{14}C and -2-^{14}C (Scheme 5). In the scheme the radicals are indicated, for simplicity, with an interrupted valence bond, whether they are actual free radicals formed by homolytic decomposition or ionic-type radicals due to heterolytic decomposition.

The new transamination process appears to be much more efficient than the conventional one, on account of the variety of amino compounds to which it can give rise.

As an example we may compare the possibilities of the system glutamic acid + oxalacetic acid within the framework of conventional transamination with those of the analogous system glutamic acid + succinic acid within the framework of radical transamination. In the former case only aspartic acid can be obtained, whereas in the latter case nine amino-acids can be formed, namely, aspartic acid, α-aminopimelic acid, γ-aminopimelic acid, α-aminoadipic acid, γ-aminoadipic acid, α-alanine, glycine, α-aminobutyric acid and γ-aminobutyric acid.

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MEASUREMENT OF FUNGICIDAL EFFECTS IN FIELD TRIALS

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DURING field trials on the control of coffee rust (*Hemileia vastatrix* B. et Br.) at the Coffee Research Station, Ruiru, Kenya, special methods were devised to obtain maximum sensitivity by minimizing the effects of localized, natural variability in rust attack intensity. These methods are of general application, and may be adapted for use with other diseases. The very considerable local variation of rust attack found is, perhaps, remarkable if, as has been generally supposed, spore dispersal is predominantly by wind. However, recent research[1–3] has shown that most air-borne spores probably do not travel far and has indicated rain-splash as important for spore dissemination.

The degree of rust infection is best expressed as the number of spore-producing, individual, infection loci per unit of leaf area and is approximately equal to the number of lesions per leaf if the proportion of overlapping mycelia is low. The relationship to the percentage of infected leaves, which is easier to determine, was examined.

A representative sample of 100 leaves was taken from five trees in each plot of a six treatment, four times replicated randomized block, spraying experiment showing considerable differences in the level of rust attack, and was recorded for the numbers of leaves having respectively one, two, three, etc., rust lesions per leaf. The lesions were generally fairly small and scattered so that undetected overlapping was negligible. The cumulative frequency distribution curves for the percentage of the total number of leaves in each category of rust lesion number per leaf were plotted on a probit scale for each plot (Fig. 1). For a low percentage of leaves infected, a straight line indicating a truncated normal distribution is approximated. As the percentage increases so the truncation is less and the degree of curvature is more pronounced, indicating increasing divergence from normality due to the greater development of the upper 'tails' of the distributions. The relation between the percentage of rusted leaves and the number of lesions per 100 leaves is thus exponential (Fig. 2) instead of sigmoid, as it would have been had the distributions remained normal. Similar results from a locality in a climatically different area showed the same relationship. Thus one measurement may be regarded as a transform of the other.

The percentage of rusted leaves may in fact be a better measure of the effect of rust attack on the tree, as evidence has been obtained of a direct relation to foliage density. Thus, in one trial, the relation between the percentage of rusted leaves in May and the number of mature leaves per mature branch (that is, one on which leaf shedding had commenced) gave a regression coefficient of $-0{\cdot}98^{**}$, that is, for each leaf rusted in May, there was nearly one less present in September. Further, in other investigations, not however concerned with rust, strong correlations between foliage density and crop yield have been found.

In order to obtain a representative sample of leaves, account must be taken of the different leaf densities in different parts of the tree. In the above investigation, a method devised for investigation of fungicide cover, etc., was used. The total number of primary branches (that is, those originating on the trunk) per tree was counted. Every second, third, etc., primary was sampled, the interval increasing with the total number present. From the trunk, a path was traced out along one side of each primary sampled, up one side of any lateral branch or lateral on this and back down the other side to its base and finally back down the opposite side of the primary, so that the whole branch system was systematically traversed. Along this path, every 10th, 20th, etc.,

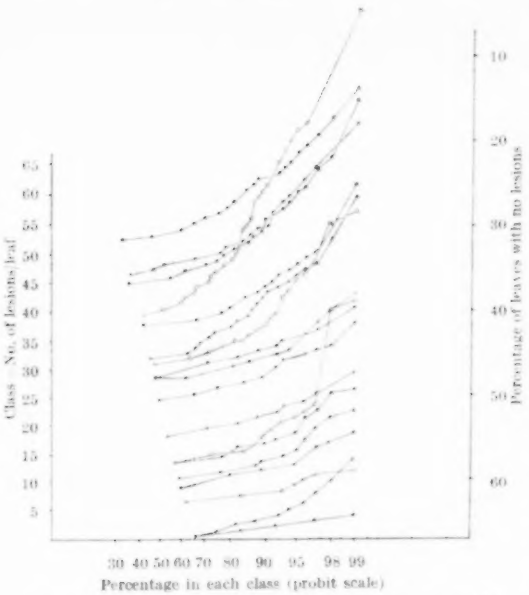
Class No. of lesions/leaf
Percentage of leaves with no lesions
Percentage in each class (probit scale)
30 40 50 60 70 80 90 95 98 99

Fig. 1. Probit cumulative frequency distribution curves for eighteen plots of coffee trees, showing the percentage of the total number of leaves examined which occurred in each 'number of lesions per leaf' class. Each curve is displaced upwards to an amount proportional to the percentage of leaves with no lesions, so as to exhibit the change in form of the curve with this latter factor

leaf passed was removed according to the size of the tree, to obtain a sample of 20–30 leaves. This was reduced to 20 by discarding at random.

For field trials a similar, but less laborious, systematic sampling system was used. Five trees in each plot were roughly divided by eye into five radial sectors and five horizontal zones. On the first tree, the lowest primary in the lowest zone was traversed as before, on the second tree the middle primary in the next sector and next zone and so on. Each mature leaf traversed was examined and recorded if attacked by rust. One hundred leaves were inspected on each primary (the adjacent primary being included if necessary), a total of five hundred leaves in each plot. The resulting percentage infection was somewhat biased by over-representation of the lower regions of the tree since these have fewer leaves. Hence some over-estimation of rust attack probably resulted since more rust occurs in this region. As

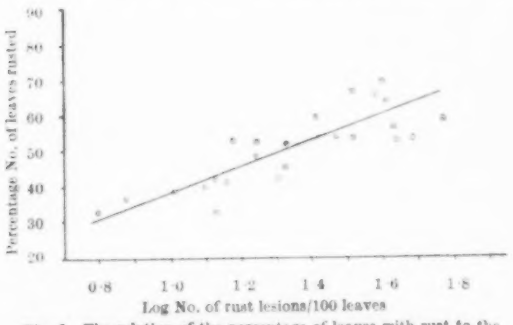

Fig. 2. The relation of the percentage of leaves with rust to the logarithm of the total number of rust leaves per hundred leaves

the trials were concerned with comparisons of treatments, this was of little importance, and it was possible for one man to record completely a large factorial trial of 42 plots and 920 trees in a few days.

That incidence of rust in the field is strongly localized is clearly shown by observations made in three field trials. In these, the design could be treated as consisting of plots of two rows of ten trees each. Rust was sampled in each row on alternate, unsprayed trees, the other trees being sprayed. The standard error between the pairs of rows (sub-plots) was considerably less than between plots, being 63·8, 44·2 and 41·9 per cent lower in the three trials. The differences between the plots were, in accordance, very highly significantly greater than would have been expected from the differences between the sub-plots. Correlation between the sub-plots is thus present, the coefficients being 0·877***, 0·522** and 0·490*** respectively. These results suggest a distribution of rust attack by dispersal from centres of infection within the area rather than by mass infection arriving from outside. The correlation between sub-plots suggests that the measurement of rust intensity on a half of each treated plot in a field trial of the effects of fungicides could be used to correct that on the treated half for local variations using covariance, and hence increase the sensitivity of the trial. The effect was measured in the trials, omitting treated trees. The standard errors were reduced by 51·1, 15·1, and 11·9 per cent. The experimental area was divided into three blocks, and some reduction in standard error was obtained from this alone (14·1, 18·3 and 0·5 per cent), but in each case using covariance additional reduction (36·3, 5·7 and 11·8 per cent) resulted. Thus the relative usefulness of the two methods for the reduction of standard error varied from trial to trial, depending on the pattern of local variation in rust intensity.

Covariance analysis, although affording a useful approximation, is not strictly applicable when treatments are actually applied, since the greater the treatment effect the lower the rust intensity and the less the effect of the unsprayed level. The regression coefficient would be expected to range from 1 to 0, varying directly with the percentage of control. This was, in fact, found to be the case when data from one trial were examined critically. The correct adjustment is thus obtained if the rust-levels on the treated halves of the plots are expressed as a percentage of those on the untreated halves. A difficulty arises if the rust-level on individual unsprayed plots falls to a level very considerably lower than is general. Small differences between sprayed and unsprayed halves will then be disproportionately exaggerated and the apparent sensitivity of the trial will be unduly decreased. The use of an index of relative disease incidence, the ratio of the differences between sprayed and unsprayed halves to their sum, which amounts to a simple transform of the percentage, was found useful in such a case.

The degree of disease control exerted by a given treatment or treatment combination over the whole trial is more precisely estimated by summing the rust intensity on the respective sprayed halves of the plots and expressing this as a percentage of that on the unsprayed halves, rather than summing and averaging the percentage reduction of rust intensity on each individual plot, these latter data being reserved to estimate the significance of the differences. Some heterogeneity of variance was found and account

was taken of this, sometimes by employing a transformation, but the effects were only slight.

The effectiveness of the methods used may be judged from the results of a factorial trial with three replications in which two fungicides at four concentrations equivalent to ¼, ½, 1 and 2 per cent Burgundy mixture were contrasted for application to upper and lower leaf surfaces. Local variation in rust attack was considerable, the coefficient for the untreated plot halves being 56·5 per cent. The linear effect of concentration was very highly significant and differences between the effects of the fungicides estimated as equivalent to those produced by the difference between 1 and 1·3 per cent concentrations were detectable. In another trial with three replications of ½, 1 and 2 per cent concentrations of three fungicides with upper and lower surface applications, differences equivalent to that between 1 and 2·6 per cent in one season and 1 and 2·1 per cent in a second season were detectable.

The observation discussed shows that intensity of rust attack may be estimated from the percentage of rusted leaves per bush, since there is evidence that this is mathematically related to the number of rust mycelia per leaf. It is probably directly related to effects on foliage density, which in turn is related to crop yield.

The sensitivity of field trials on the fungicidal control of rust disease may be considerably increased when local variation in intensity of attack is marked, by assessing this variation from estimates of rust intensity on alternate, unsprayed trees in each plot. The procedure increases the accuracy of the estimates of degree of control. Further, it should reduce the effects of any reduction in inoculum production resulting from a spray treatment on one plot on the inoculum-level in neighbouring plots.

The design was very satisfactory for differentiating between treatments where the aim was to assess the amount of protection against infection afforded by each. If, however, it is required to estimate the effects, especially as regards timing, on the rate of build-up of infection and this is influenced to any considerable extent by the amount of inoculum movement from tree to tree, the method may be unsatisfactory except for estimating 'within tree' effects and the amount of the inoculum movement. A method of dealing with this difficulty might be to use square plots in which the effect of varying the number of trees in a central sprayed group surrounded by unsprayed trees would be determined, and allowance made for the estimated effects of area sprayed on rate of build-up of attack by the disease.

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PREDICTION OF THE EFFECT OF LIGHT-TIME FRACTION ON THE CRITICAL FLICKER FREQUENCY; AN INSIGHT FROM FOURIER ANALYSIS

By K. GIBBINS and Dr. C. I. HOWARTH
Department of Psychology, University of Hull

THE study of the response of the human eye to flickering light has notoriously produced a number of extremely complex and confusing results. This article shows how at least part of the confusion can be resolved by the application of simple physical principles to the problem. At least two workers[1,2] have commented recently on the particularly chaotic results found in investigations of the relationship between the light-time-fraction (L.T.F., sometimes misleadingly called light-dark-ratio) and the critical flicker frequency (C.F.F., that is, the fastest frequency at which flicker is just perceptible). A sample of these results as summarized by Landis[3] is shown in Fig. 1. We suggest that the confusion can be understood and ordered by considering the Fourier analysis of the stimuli with different L.T.F.'s. In the present case, all we wish to do is to point out that a train of stimuli near fusion (the C.F.F. condition) can be considered to contain two different components: (*a*) a steady component (the first Fourier component) which is the mean intensity of the light and which we shall call I_M; (*b*) a fluctuating component (consisting of the second and higher Fourier components). This we shall call I_F.

The steady term I_M can be considered as a background illumination (or adaptation-level) and must have the effect of masking the fluctuating part, I_F, and thus of reducing the C.F.F. if I_F is held constant. I_F, on the other hand, is the effective stimulus and for a constant I_M, increasing I_F must increase the C.F.F. The crux of our argument is that complementary L.T.F.'s (for example, 0·1 and 0·9, or 0·3 and 0·7) are identical in the amplitude of their flickering components but differ in the amplitude of the steady components; 0·9 L.T.F. is much brighter than 0·1 L.T.F. since its I_M is nine times greater. Two things follow from this. First, we would predict that if the reduction in I_M for short L.T.F.'s is compensated by the addition of a steady light to the flickering light, the C.F.F. for complementary L.T.F.'s should be equal. Secondly, if we knew the effect of changing I_M, while holding I_F constant, we should be able to predict the shape of the curve of L.T.F. against C.F.F. for the uncompensated condition.

Other workers[4-6] have attempted to compensate for the obvious difference in brightness by varying the intensity of the flickering light. In our terms this is an illogical procedure, since, although I_M is now held constant, I_F varies inversely with the L.T.F. It is therefore not surprising that all these workers found C.F.F. higher for 0·1 L.T.F. than for 0·9. If no compensation of any kind is attempted, 0·1 still usually has a higher C.F.F. than 0·9. In this case it is because I_M varies with L.T.F. and the higher I_M masks the constant I_F and hence reduces the C.F.F.

To test our hypothesis we have repeated the experiments reported by previous workers and have managed to obtain most of the forms of relationship reported previously. Then we compensated by adding

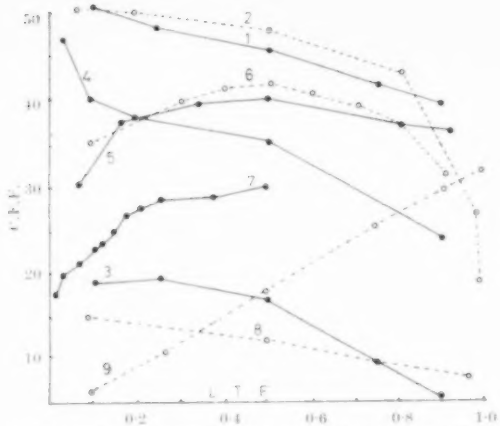

Fig. 1. Landis's (1954) summary of previous data. Effect of L.T.F. on C.F.F. as reported by different investigators. 1, Cobb, P. W., *J. Opt. Soc. Amer.*, **24**, 107 (1934); 2 and 3, Crozier, W. J. and Wolf, E., *J. Gen. Physiol.*, **24**, 505 (1941); 4 and 5, Bartley, S. H., *J. Exp. Psych.*, **21**, 678 (1937); 6 and 8, Ives, H. E., *J. Opt. Soc. Amer.*, **6**, 254 (1922); 7, Porter, T. C., *Proc. Roy. Soc. A*, **70**, 313 (1902); 9, Pieron, H., *C. Rend. Soc. Biol.*, **99**, 398 (1928).

It should be noted that curve 9 is not entirely accurate. Pieron gives no percentage light per cycle (L.T.F.) but percentage dark per cycle. With L.T.F. as co-ordinate the curve should be reversed. It is, in fact, entirely compatible with curves 8, 3, 2, for example

a steady light of such an intensity that for all the L.T.F.'s we used the I_M was equal to that of the 0·9 L.T.F. As we expected, this resulted in complementary L.T.F.s having the same C.F.F. no matter what the shape of the uncompensated curve. A selection of our results is shown in Fig. 2. It adds to our satisfaction that in those cases where the uncompensated curves are symmetrical, our compensation has no effect and the curves remain symmetrical.

The bow-shaped symmetrical curve is also to be expected from the Fourier analysis. If one assumes (as one very plausibly may near the C.F.F.) that only the first flickering component of the Fourier analysis is effective, then one would expect the relationship of C.F.F. to L.T.F. to follow the relationship between the amplitude of the first flickering component and the L.T.F. This latter is, in fact, a simple bow-shaped curve with a maximum at 0·5 L.T.F.

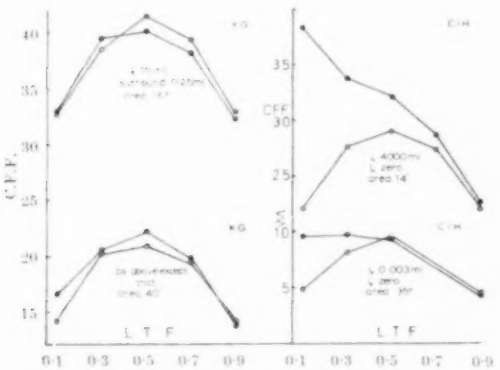

Fig. 2. The effect of changing the light-time-fraction on the critical flicker frequency. Filled circles represent mean C.F.F. with L.T.F. uncompensated for mean intensity. Empty circles represent mean C.F.F. with L.T.F. compensated so that the mean intensity is that of the uncompensated 0·9 L.T.F. This was done by adding a steady light to the remaining L.T.F. stimuli

We have already mentioned that the degree of asymmetry of the uncompensated curve should be predictable if one knew the relationship between I_M and C.F.F. for a given I_F. Complete data on this do not exist, but a very plausible deduction can be made from the very extensive data on the relationship between I_M and C.F.F. when I_F varies with I_M keeping I_F/I_M constant. This is, in fact, the usual way in which the relationship between C.F.F. and stimulus intensity has been obtained, using square waves of variable intensity with no background. Typically C.F.F. increases linearly with log I except for two regions where intensity has little or no effect on C.F.F.; see, for example, Hecht and Smith[7]. The first of these occurs at about 0·001 ml. between the photopic and scotopic regions, the second occurs at very high intensities, about 1,000 ml., where the direction of the relationship may actually reverse. Between these two regions C.F.F. increases markedly with intensity. In the two regions where intensity has little influence on C.F.F., the effect of I_F in increasing the C.F.F. and of I_M in decreasing it must almost exactly balance. In between, the effect of I_F is relatively greater. If we assume that this is because I_M is having a smaller effect in the intermediate region, then we would expect the least degree of asymmetry in the C.F.F.–L.T.F. curves under this condition. The two curves on the left-hand side of Fig. 2 were, in fact, obtained in this region, and the slight effect of area which they show fits the greater effect of increasing intensity for the larger areas. The two regions where intensity has little effect on C.F.F. would be expected to produce the greatest degree of asymmetry since here we have supposed that I_M will be exerting its greatest effect and the asymmetry is due to the change of I_M with L.T.F. in the uncompensated condition. The two curves on the right of Fig. 2 were obtained under these conditions.

There remains the possibility that the regions in which intensity has little effect on C.F.F. are due not to a change in the effectiveness of I_M but to a change in the effectiveness of I_F. However, de Lange[8] has published enough data to make this seem extremely unlikely although his data do not quite cover the necessary intensity range. The present experiments, of course, show that at 0·001 ml. and at 1,000 ml. I_M has a considerable influence on C.F.F., while at 1·5 ml. it has almost no effect.

The application of Fourier analysis to physical systems with a limited frequency response is strictly possible only for linear systems. There is a great deal of evidence that the eye, like most other sense organs, is non-linear in its response. However, there are many non-linear systems where the analysis of square wave impulses can give useful information provided not too much is expected of it. In the present case we have made only the most elementary use of the concepts of Fourier analysis. How far the method can be extended remains to be seen.

We wish to thank the Director-General of Medical Services for permission to publish this paper.

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LETTERS TO THE EDITORS

RADIOPHYSICS

Some Preliminary Experimental Tests of a Novel Method of Radiating at Very Low Frequencies

For some years the idea of using an island as a radiator of very low frequencies (VLF) has been discussed in this Establishment. A long, narrow island some 20 miles by 1 mile, composed of poorly conducting material, would be ideal for the purpose. A narrow peninsula would provide a somewhat less efficient radiator. There are some similarities with the slot aerial, but the analogy cannot be pressed too far.

Experiments have recently been carried out using a peninsula some 10 miles long. A cable was laid across its root and the ends of the cable earthed in the sea. Power was fed into the mid-point of the cable.

If it is assumed that the island or peninsula is sufficiently narrow for the far-field to be determined by the algebraic sum of the currents on either side of it, then for radiation purposes a standing wave pattern of a half-wave dipole, or a correctly phased series of them, could be produced. Sufficiently low lobes might then be expected from a large enough array to launch very low-frequency waves at an angle suitable for long-range propagation. In the present trials it is quite probable that the major part of the radiation passed well above the receiving sites investigated, and returned to earth at much greater ranges.

Of several sites considered for the preliminary work, the Loch Long Gareloch area offered the most advantages. Fig. 1 shows the position of the earthing plates *P*1 and *P*2. The earthing plates consisted of thin copper sheets 6 ft. × 3 ft., mounted on wooden frameworks. Three such plates spaced about 50 yards apart were used in each Loch. They were suspended near the surface with the aid of a system of buoys. The cable used was ordinary power cable of which approximately 3,000 yards were laid.

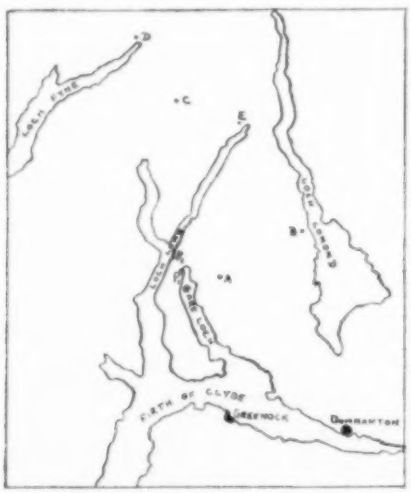

Fig. 1. Trials area

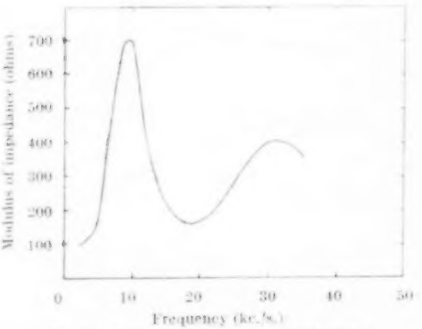

Fig. 2. Total path-impedance at high water

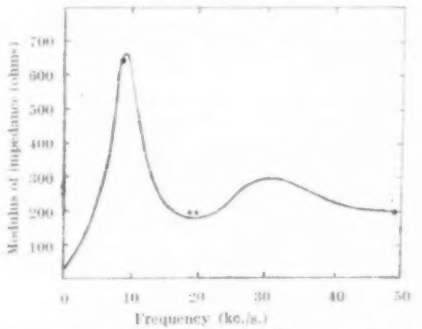

Fig. 3. Total path-impedance. ——, between high and low water; ●, at low water

The transmitter delivered 50 watts at a frequency of 10 kc./s. The signals were received on a standard communications receiver with a high-*Q* ferrite loop aerial.

The objects of the initial experiments were to determine the suitability of such a peninsula for a radiator of very low frequencies and to determine its impedance characteristics.

Although the atmospheric noise appeared to be abnormally high, the signal was received at points *A*, *B*, *C*, *D* and *E*, shown in Fig. 1. At these points the receiving loop aerial could be used to obtain the approximate bearing of the transmitting aerial, and in each case this bearing appeared to point towards the centre of the sea-path. This was true, even at point *A*, when the receiving loop plane was rotated about a vertical axis: however, at *A*, reception was also achieved with the plane of the loop horizontal, which was not the case elsewhere.

It was expected that when the total length of current-path was an odd number of half wave-lengths the impedance would be high, whereas when the path-length was an even number of half wave-lengths the impedance would be low. Impedance

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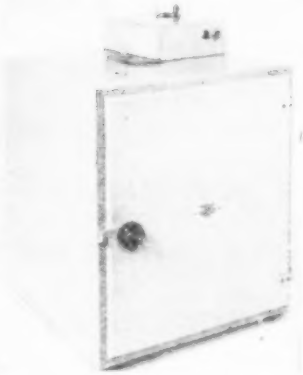

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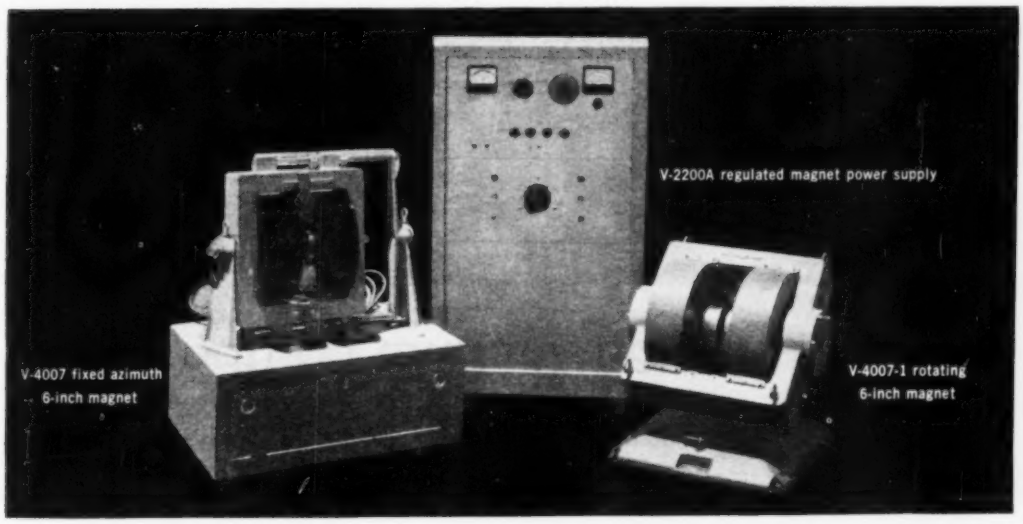

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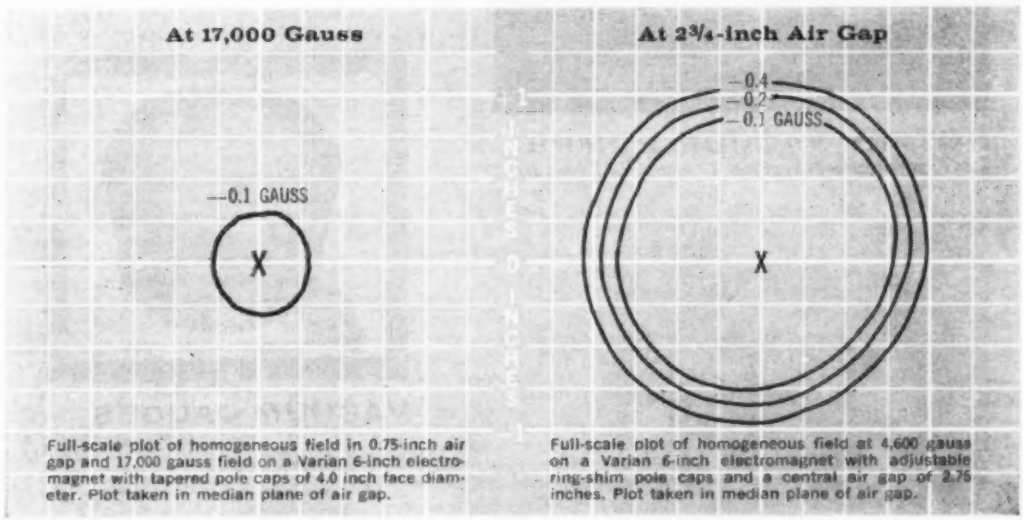

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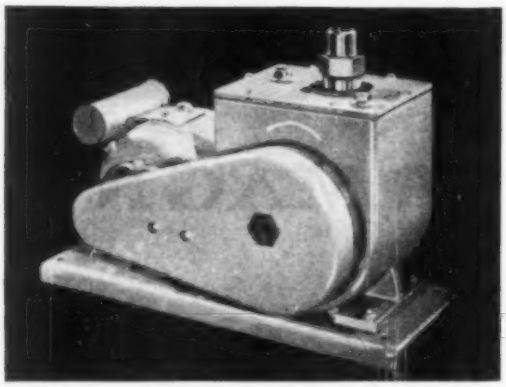

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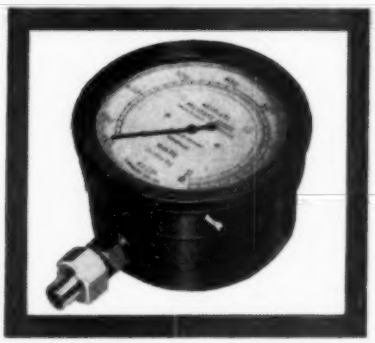

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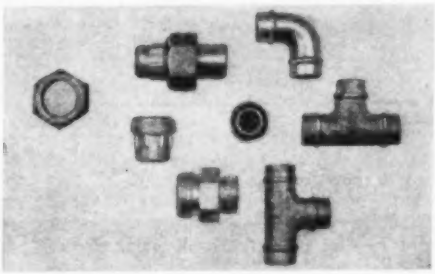

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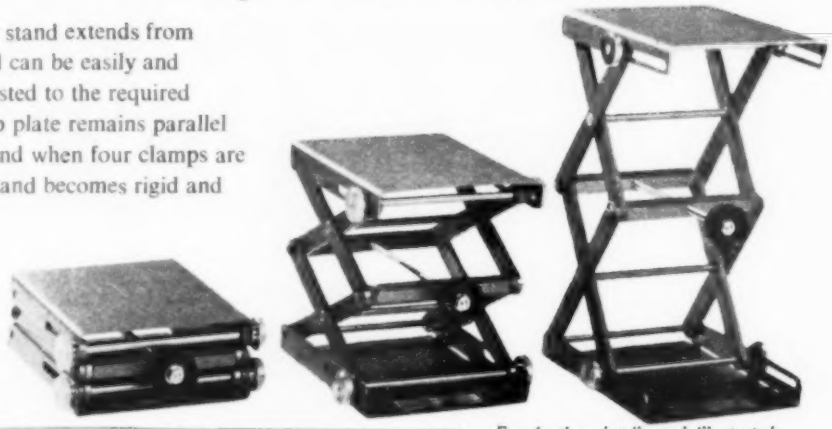

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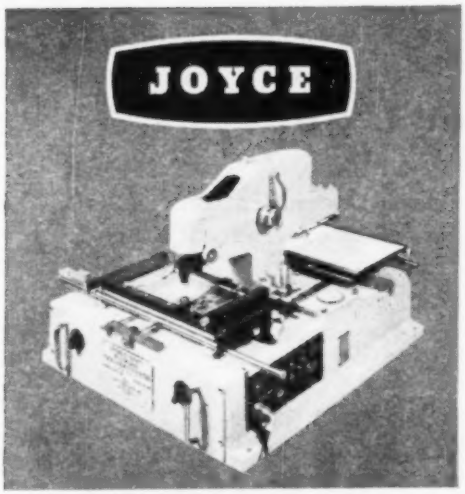

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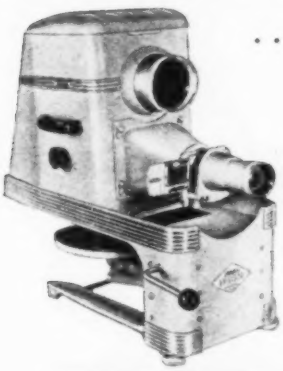

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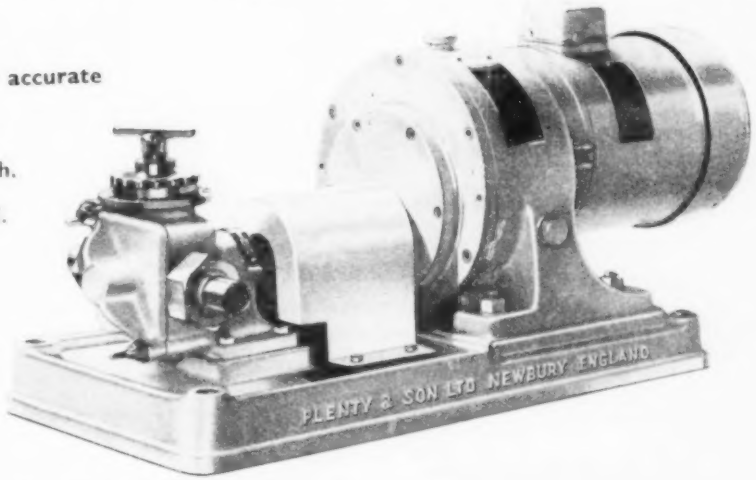

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minima were therefore expected, due allowance being made for the measured path-length, at integral multiples of 10 kc./s. and impedance maxima at odd integral multiples of 5 kc./s. As shown in Figs. 2 and 3, a maximum occurred at 10 kc./s. and a minimum at 20 kc./s. From subsequent experiments it appears that the effect arises on account of changes in the characteristics of the cable due to the proximity of the ground with which it was in contact.

It is concluded that the experiments clearly demonstrate the feasibility of the present proposals, as genuine radiation effects were observed. Some attention must, however, be paid to reducing the cable capacity to earth and the associated losses.

In conclusion, it should be mentioned that during these first trials, Press reports appeared of a similar investigation in Antarctica which had a rather different objective.

Thanks are due to Messrs. R. Benjamin, A. T. Rawles and K. V. Watt, of this Establishment, for useful discussions, to Messrs. W. R. Carter, W. L. Hibbens and E. G. Richards for assistance in the trials, and to the Admiralty for permission to publish the results.

R. N. Gould

Admiralty Surface Weapons Establishment,
Portsdown, Cosham,
Portsmouth, Hants.

ASTROPHYSICS

Minimum Range to Artificial Earth Satellites

A PREREQUISITE for ionospheric work with satellites by means of the Doppler method is the knowledge of the behaviour of the Doppler-frequency shift in free space. A free-space condition prevails, if the operating frequency f is much greater than the maximum plasma frequency. It is the purpose of this communication to present in a general form an equation from which the minimum range between a satellite S and an observer P can be determined and to illustrate the magnitudes of higher-order terms.

The first reports which appeared in the technical literature regarding the minimum-range equation generously neglected the effects of the curvature of the satellite orbit. An equation which included the effects of this curvature has been reported[1]. Specific reference to the previous neglect has been made by Brito[2] and in a simplified form by me[3]. Priester and Brito took into account the relative velocity between source and observer, but neither equation was complete. To arrive at a complete expression for the minimum-range equation, I shall first consider a two-dimensional case with the observer at rest ($v_p = 0$) in the plane of the orbit of S. In this case, one obtains the following equation for the time-derivative of the Doppler-shift curve for $v_s/c \ll 1$:

$$\lambda \dot{f}' = -\frac{v_s^2}{R}\sin^2\psi + \frac{v_s^2}{\rho_s}\cos\alpha \qquad (1)$$

where $\lambda = c/f$, c is the velocity of light in free space and f is the transmitter frequency of the satellite, $\dot{f}'$ is the time derivative of the frequency f' received at P, v_s is the orbital speed, R is the range SP, ρ_s is the radius of the orbit of S, $\psi = \sphericalangle \vec{v}_s \vec{R}$, and $\alpha = (\pi/2 - \psi)$. In the limit equation (1) assumes the form (when $\psi = \pi/2$, $\alpha = 0$, $R = R_m$):

$$\lambda(\dot{f}')_{\max.} = -\frac{v_s^2}{R_m} + \frac{v_s^2}{\rho_s} \qquad (2)$$

or

$$\lambda(\dot{f}')_{\max.} = -\frac{v_s^2}{R_m} + \frac{v_s^2}{\rho_s}\cos\xi \qquad (3)$$

if P is outside the plane of the orbit[4], ξ is the angle between $\vec{\rho}_s$ and $\vec{R}_m$ and R_m is the minimum range between S and P. In equations (1), (2) and (3) the second terms on the right represent the components of a radial acceleration toward P.

An earth-based observer at P, who is not located at the poles, is in orbital motion ($v_p \neq 0$) due to the spin of the Earth around its axis. Consequently, the minimum-range equation contains an additional radial acceleration component and can be written as:

$$\lambda(\dot{f}')_{f'=f} = -\frac{v_{\mathrm{rel.}}^2}{R_m} + \frac{v_s^2}{\rho_s}\cos\alpha - \frac{v_p^2}{\rho_p}\cos\beta \qquad (4)$$

where

$$v_{\mathrm{rel.}}^2 = v_s^2 + v_p^2 - 2v_s v_p \cos j,\ j = \sphericalangle \vec{v}_s \vec{v}_p,$$
$$\alpha = \sphericalangle \vec{\rho}_s \vec{R}_m,\ \beta = \sphericalangle \vec{\rho}_p \vec{R}_m$$

with the signs in (4) corresponding to $\alpha, \beta < \pi/2$. It is seen that $\lambda(\dot{f}')_{f'=f}$ which may be different from $\lambda(\dot{f}')_{\max.}$ is equal to the sum of three accelerations. The first term represents the radial acceleration due to a rotation of S with $\vec{v}_{\mathrm{rel.}}$ perpendicular to $\vec{R}_m$. Since R increases for any displacement from $R = R_m$, the sign of the first term is negative. The second and third term represent the components of a radial acceleration for the satellite (v_s^2/ρ_s) and for the observer (v_p^2/ρ_p) in the direction of $\vec{R}_m$.

For $\rho_s = \rho_s = \infty$, including now the relativistic correction, one obtains the minimum-range equation for linear orbits:

$$\frac{\lambda(\dot{f}')_{f'=f}}{\sqrt{1 - \left(\frac{v_{\mathrm{rel.}}}{c}\right)^2}} = -\frac{v_{\mathrm{rel.}}^2}{R_m} \qquad (5)$$

For satellite orbits the relativistic correction amounts to about four parts in 10^{10}. For practical purposes equation (4) seems adequate, since this correction corresponds to a quality of measurement equivalent of resolving less than 1 mm. of a 1,000-km. range.

The orbital motion of S and P may not be circular. Moreover, since the Earth is moving around the Sun ($v_G \doteq 30$ km./sec.) and since the Sun is moving in a curved orbit ($v_H \doteq 230$ km./sec.) around a centre of curvature, and since our Galaxy may move in its own curved path, etc., one can, for theoretical completeness, write the minimum-range equation in a form which includes all possible velocity and acceleration components. For $v_{\mathrm{rel.}} \ll c$ this leads to the scalar equation :

$$\lambda(\dot{f}')_{f'=f} = -\frac{v_{\mathrm{rel.}}^2}{R_m} + \sum_i\left(\frac{v_{is}^2}{\rho_{is}}\cos\alpha_i - \frac{v_{ip}^2}{\rho_{ip}}\cos\beta_i\right) + \sum_i(\dot{v}_{is}\cos\gamma_i - \dot{v}_{ip}\cos\delta_i) \qquad (6)$$

where in vector form, $\vec{v}_{\mathrm{rel.}} = \sum_i(\vec{v}_{is} - \vec{v}_{ip})$ and the signs in equation (6) correspond to $\alpha_i, \beta_i, \gamma_i, \delta_i < \pi/2$. i is an index which refers the motion of S (satellite) and P (observer) to centres of curvature in the systems of the Earth, Sun, Galaxy, etc., respectively. In equation (6) both summations

contain components of radial and tangential accelerations in the direction of R_m.

Since the magnitudes of the higher-order terms (Sun, Galaxy, etc.) are less than 10^{-9} times the first term in equation (6) the slope of the Doppler-shift curve can be said to contain detectable and 'undetectable' elements of motion. The cause of the 'undetectable' motions reaches deep into space. For the detectable motions equation (4) seems sufficient. An estimate of the significance of each component of (4) reveals that for S and P orbiting, for example, in the equatorial plane with S at 1,000 km. elevation, the error introduced in R_m by neglecting the curvature of the orbit of S is about -15 per cent, while the error introduced by neglecting the curvature of the orbit of P is about $+0{\cdot}1$ per cent. If the slope of the Doppler-shift curve can be measured to an accuracy better than about 0·1 per cent, the latter contribution cannot be neglected. This does not mean, however, that with less accuracy the contribution due to the radial acceleration of P vanishes. If P is located at either pole of the Earth, $v_p = 0$ and equation (3) is valid for P outside the plane of the orbit of S.

K. Toman

A.F. Cambridge Research Laboratories,
Bedford, Massachusetts.

[1] Priester, W., and Hergenhahn, G., *Bahnbestimmung von Erdsatelliten aus Doppler-Effekt-Messungen*, 18 (Westdeutscher Verlag, Köln und Opladen, 1958).
[2] Brito, J. M., *Proc. Inst. Rad. Eng.*, **47**, 2023 (1959).
[3] Toman, K., *Proc. Inst. Rad. Eng.*, **48**, 1339 (1960).
[4] Toman, K., *Proc. Inst. Rad. Eng.* (in the press).

PHYSICS

Confining a Plasma in Steady Electric and Magnetic Fields

I have suggested that ions may be trapped in an electric potential-well situated in a magnetic field[1]. The basic field configuration proposed was analogous to that in the Penning or Philips ion gauge discharge[2], where electrons are trapped, say, between two cathodes for a comparatively long period before they reach the anode ring situated between the cathodes. For trapping ions, the required potential-well is produced, for example, if a cathode ring is situated between two anode plates, with a magnetic field parallel to the axis of the cathode.

Experimental work was undertaken to study this possibility. The main experimental difficulty in realizing a field configuration suitable for confining ons was due to the fact that ions had to be generated by auxiliary discharges in regions adjacent to, but different from, the trapping region and had to be drawn into the latter region. In the case of Penning discharge, the electron current is initiated in the trapping region itself by field emission from the cathode or by ionization produced by cosmic or other background radiation.

Deuterium was used in these experiments, because the neutrons emitted by D–D reactions served as the indicator for the study of the plasma produced. Recent experiments were carried out at a gas pressure of a few microns of mercury. The voltage used for the discharge varied from 10 to 20 kV., and the discharge current was 5–10 m.amp. The magnetic field available was about 1,700 gauss.

Three main results were obtained as a result of this work: (*a*) The emission of neutrons indicated that high-energy ions were produced in this discharge. (*b*) By scanning the region of the discharge with a neutron detector provided with neutron collimation, it was found that the neutrons were mainly from the discharge region and not from the electrodes. (*c*) The most important result was that there was evidence for confinement of the ions. Because of the uncertainty in estimating the ionic component of the discharge current and the effective ion density, an estimate of absolute efficiency of neutron production was only of dubious value at the present stage of the experiment. Therefore, comparative neutron yields at different voltages were determined, with other parameters kept constant. If there were no confinement of the ions one would expect that the relative yield should follow the theoretical Gamow curve which has been experimentally verified[3–5]. On the other hand, if there were any confinement, the lower-energy ions would be confined relatively more than the higher energy ions, even in this very limited magnetic field. This meant that a graph of neutron yield at different voltages, when normalized at a particular energy on the Gamow curve, should show relatively larger yield at lower energies. Indeed, this was observed (Fig. 1). The solid line shows the variation of D–D reaction cross-section with energy[4], and the dashed line represents the relative yield of neutrons in the present experiments, at different voltages, normalized at 16 kV.

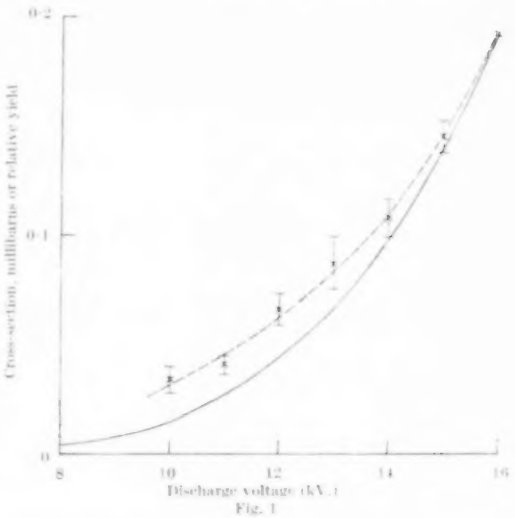

Fig. 1

Work is being continued, and the experimental details will be published elsewhere.

I am grateful to my colleagues Mr. S. S. Samant for assistance in the experimental work, Mr. M. L. Uplekar for the construction of some equipment, and Dr. A. P. Thatte and Mr. S. S. Bhave for useful discussions. I thank Prof. D. Y. Phadke for his encouragement.

K. A. George

Tata Institute of Fundamental Research,
Colaba, Bombay-5, India.

[1] George, K. A., *Controlled Thermonuclear Power* (1958, unpublished).
[2] Penning, F. M., *Physica*, **4**, 71 (1937).
[3] Arnold, W. R., *et al.*, *Phys. Rev.*, **93**, 483 (1954).
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A Proposal for increasing the Beam Output from a Synchrocyclotron

In this communication, the possibility is considered of appreciably increasing the mean output of a synchrocyclotron, using relatively inexpensive equipment and with the expenditure of only a small amount of electrical power.

Suppose that a small dee system, covering the orbits of ions with energies of up to about 5 MeV., is placed opposite the live dee at the centre of the machine. To this small additional dee a high-voltage radio-frequency signal is fed which is in antiphase to that on the main dee. This signal is derived from the main oscillator system after amplification in a separate power amplifier. The auxiliary amplifier is pulsed on at a time slightly before the main dee commences to capture ions from the ion source, and is switched off when the captured ions have gained on the average a few MeV., that is, when the ion bunch is circulating at a radius such that it truly enters the main dee electrode and thus picks up the full dee voltage. It is essential that the auxiliary dee signal is reduced to a very small value as the ion bunch approaches the radius of the small dee edge, to avoid inducing radial betatron oscillations.

In Fig. 1 the assumed variation of the energy gained per turn by an ion is shown as a function of the orbit radius. Three cases are shown: the first curve corresponds to a normal synchrocyclotron, and the second curve to a machine modified in the way here described. The third curve, produced by too large a voltage on the small dee, is probably undesirable, because ions captured into stable orbits at the peak of the curve would afterwards be lost. Obviously, to achieve the required shape of the curve, the auxiliary power amplifier output must be gradually tapered off.

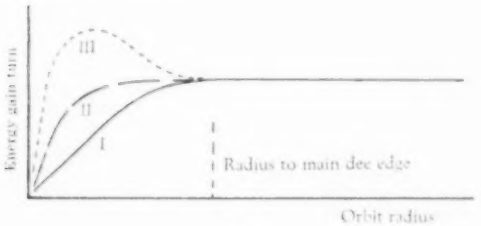

Fig. 1

The manner in which such an arrangement could produce an increase in the intensity of the beam is now considered. First, the energy gained per turn by the ions would be increased, permitting the use of a larger area in phase-space for ion capture. Secondly, the ions would be extracted more rapidly from the region of high particle density near the ion source, with a consequent reduction in the number of ions lost by gas scattering. Thirdly, the production of a more uniform electric field in the central region would cause a reduction in the movements of the centres of the orbits away from the centre of the machine, thereby reducing the amplitudes of the radial betatron oscillations.

The band-width and power requirements of the auxiliary amplifier are quite modest; a power of 1–2 per cent of the main oscillator power is sufficient, and the band-width need only cover the range of synchronous frequencies required by the ion bunch

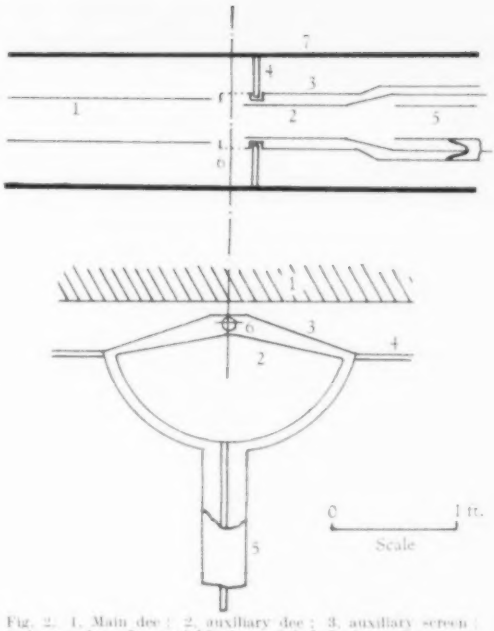

Fig. 2. 1, Main dee; 2, auxiliary dee; 3, auxiliary screen; 4, dummy dee; 5, co-axial feeders; 6, hole for ions; 7, vacuum chamber walls

in its passage from the source to the radius at which the auxiliary amplifier is switched off. So that large signals are not induced in the small dee system by the main dee when it is switched off, the feed line should be resistively loaded; but this is usually also required to achieve a sufficiently wide band-width. In addition, a small earthed screen between the main dee and the auxiliary dee is desirable to reduce the electric coupling between the two dees and to improve the shape of the field near the centre of the machine. A typical arrangement is shown in Fig. 2.

Preliminary tests of this scheme have been made with the Harwell 110-in. synchrocyclotron, using an 11-in. radius dee with a total operating time of approximately 50 μsec. in each main modulation cycle. The rate of repetition for this machine is 200 c./s. A peak voltage of 4 kV. was used on the small dee, the main dee voltage being approximately 8 kV. peak. Despite a reduction in the vertical aperture of 25 per cent, caused by the small dees, an increase in the beam current measured at 50 meV. of approximately 60 per cent was readily achieved.

I thank the members of the team engaged on this work, in particular P. S. Rogers, for their help, and also J. D. Lawson for helpful discussions.

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Effect of a Resisting Couple on the Rotational Motion of a Rigid Body

In a recent communication[1], Nonweiler demonstrates the proposition that an external couple applied to a rigid body about its instantaneous axis of rotation in the sense opposing its rotation tends to cause the axis to approach the axis of greatest

moment (provided that the instantaneous axis is not initially that of a permanent rotation). He refers to the rotational motion of artificial Earth satellites and the manner in which their instantaneous axes of rotation have been observed to approach the axis of greatest moment and suggests that this theorem may be relevant.

It seems to me, however, that if the underlying assumption of Nonweiler's proposition, that the external couple **G** is opposite to the angular velocity vector **w**, is interpreted in the usual sense, $\mathbf{G} = -k\mathbf{w}$ (k, positive), then it does not, in general, apply to bodies under the influence of aerodynamic damping moments. In most practical cases, we are concerned with bodies having axial symmetry, and the damping moment about the axis of symmetry will be quite small compared with the damping moment about a lateral axis; in other words, the spin will tend to be retained whereas angular motions in pitch and yaw will be damped. Thus, whereas the direction of **G** will be such that **G.w** is negative, the more restrictive condition $\mathbf{G} = -k\mathbf{w}$ will not apply. The only case to which the theorem as stated is directly applicable is that of a body, such as a sphere, having inertial asymmetry, but equal damping derivatives about three orthogonal axes.

Nonweiler derives the equation:

$$\frac{\mathrm{d}}{\mathrm{d}t}(h^2/2T) = \tfrac{1}{2}(\mathbf{G} \times \mathbf{h}).(\mathbf{h} \times \mathbf{w})/T^2 \qquad (1)$$

where **h** is the vector moment of momentum and T the kinetic energy of rotation. He shows that an increasing value of $(h^2/2T)$ may be interpreted as a movement of the instantaneous axis of rotation towards the axis of greatest moment. Now the term $(\mathbf{G} \times \mathbf{h}).(\mathbf{h} \times \mathbf{w})$ is positive if, and only if, the component of **G** in the plane of **w** and **h** is directed towards the side of the line of action of **h** opposite to **w**. This includes the particular case $\mathbf{G} = -k\mathbf{w}$, but does not include the more general condition that **G.w** is negative, satisfied, in practice, by an aerodynamic resisting couple. For this latter case, the conclusion may be rather different. Instead of the instantaneous axis of rotation tending to approach the axis of greatest moment, it will in most practical cases tend to approach the axis of symmetry, whether this is the axis of greatest moment or not. For example, a long pencil-like object spinning about its axis of symmetry and subjected to a resisting couple would be stable and not unstable as Nonweiler's proposition might imply. The fact that the converse behaviour has been observed on artificial Earth satellites would suggest that they are not in fact behaving as rigid bodies and that the role of internal energy dissipation is a dominant one.

The result for this more general condition may best be seen by resolving the vectors along principal body axes. Thus, writing:

$$\mathbf{w} \equiv (p,q,r)$$

$$\mathbf{G} \equiv (-\lambda p, -\mu q, -\nu r)$$

equation (1) becomes:

$$\frac{\mathrm{d}}{\mathrm{d}t}(h^2/2T) = \Sigma q^2 r^2(\nu B - \mu C)(B - C)/T^2 \qquad (2)$$

where (A, B, C) are the principal moments of inertia and the summation is taken over all three components.

This equation could be used to indicate the motion of the instantaneous axis of rotation in any particular case, but no general interpretation can be given. However, for an axisymmetric body, we may put $\nu = \mu$, $C = B$ and equation (2) reduces to:

$$\frac{\mathrm{d}}{\mathrm{d}t}(h^2/2T) = p^2(q^2 + r^2)(\mu A - \lambda B)(A - B) \qquad (3)$$

In most practical cases, μ will be large compared with λ so that $(\mu A - \lambda B)$ will be positive. The sign of $\frac{\mathrm{d}}{\mathrm{d}t}(h^2/2T)$ will then be determined by that of $(A - B)$. Thus for $A > B$, $h^2/2T$ will increase and the instantaneous axis of rotation will tend towards the axis of greatest moment, that is, the x axis, which is the axis of symmetry. If $A < B$, $h^2/2T$ will decrease and the axis of rotation will tend towards the axis of least moment, that is, again towards the x axis. Thus it will always move towards the axis of symmetry provided that the condition $\mu A > \lambda B$ is satisfied.

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Anomalous Thermoelectric Properties of Gadolinium Selenide

An earlier paper[1] has shown a narrow range of composition in the gadolinium–selenium system to exhibit highly interesting thermoelectric figures of merit ($Z = 4{\cdot}5 - 6{\cdot}0 \times 10^{-2}$ at 800° C.) The composition attaining such values lies between the two compounds GdSe and Gd_2Se_3, the characteristics of which have been summarized[2] as follows:

GdSe: NaCl type structure, bonding essentially covalent, very low electrical resistivity, Seebeck coefficient ~ 10 μV./deg. C.

Gd_2Se_3: defect Th_3P_4 type structure, bonding essentially ionic, very high electrical resistivity, Seebeck coefficient ~ 300 μV./deg. C.

High thermoelectric figures of merit are obtained when the preferred composition (~ 90 per cent Gd_2Se_3) has been quenched from temperatures just above the melting point (~ 1,800° C.), but these are lost on remelting or slow cooling from the melt. The parameters (Fig. 1) from which Z is calculated in the preferred composition present several interrelationships which are anomalous in the light of normal thermoelectric semi-conductor theory[3]. A detailed paper, to be submitted elsewhere, attempts to correlate and explain these anomalies.

Examples of the anomalies in the gadolinium–selenium composition are as follows: the increase in Q values with temperature suggests that the material is impurity-degenerate; but this does not conform with the linear or slightly decreasing values of $\varkappa$ which indicate non-degeneracy. The normal comparison between ZT and Q^2/L is not found. Up to ~ 800° C., $\varkappa_{ph}$ is proportional to reciprocal temperature, but above this the relationship $\varkappa = \varkappa_{el} + \varkappa_{ph}$ obviously does not apply. Derivation of $\varkappa_{el}$ from ρ values through the Wiedemann–Franz relationship is inadmissible, because the system is heterogeneous, as indicated by a plot of ρ vs. T. Normal X-ray diffractometry and metallography show, however, the material to be essentially single phase, and indeed when two phases are obviously present the material loses its high Z values.

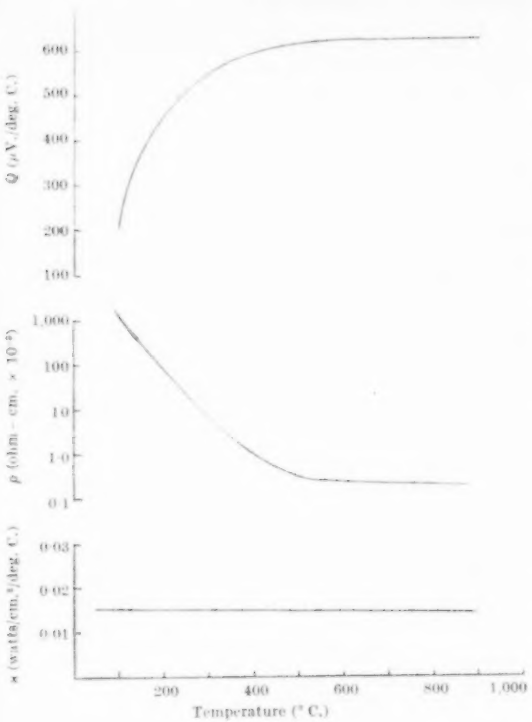

Fig. 1

Duwez *et al.*[4] have recently shown that, under conditions of rapid quenching from high temperatures, metastable and previously unknown intermetallic compounds are found in alloy systems. Similar work has been reported by Russian workers and summarized by Yevseyev[5]. In the present system, it is now believed that, under appropriate conditions of preparation, GdSe and Gd_2Se_3 interact to form such a metastable compound. This metastable product is believed to involve a lattice interaction through which the covalently bound GdSe and the ionically bound Gd_2Se_3 share a common crystal plane boundary. The bonding across such a boundary must be visualized as existing in a highly resonant condition; preliminary calculations suggest a room temperature resonance frequency of $\sim 4{\cdot}6 \times 10^{17}$ sec.$^{-1}$.

The essentially ionic nature of the predominant Gd_2Se_3 component, and the presence of the bounding plane postulated can be expected to present some resistance to the passage of carriers of electrically stimulated charge unless a novel transport mechanism is involved. This we now feel can be rationalized, on the basis of the phenomenon observed, by visualizing electromagnetic waves of thermal frequency—'thermons'—as charge carriers, and these associated with an almost purely inverse temperature-dependent variation in frequency of bonding resonance. Consequently, 'thermons' of a given frequency will not penetrate the resonance barrier until, by thermal vibration, the resonance frequency has decreased to the point at which the incident wave and the resonance oscillation are in harmony. At this point 'thermons', carrying the electrical charge, will avalanche through the barrier and electrical resistivity will drop.

Considering further the function of thermons in terms of Seebeck coefficient, we can visualize their passage through the resonating barrier in terms of oscillator-wave interaction theory, from which it is expected that energy will flow to or from the incident thermons, depending on resonance or otherwise of the bonding frequency (oscillator) and the incident frequency (wave). We believe, therefore, that the remarkably high Seebeck coefficient of such lattice-interacted gadolinium selenide can be attributed to the acquisition by incident thermons of energy from this resonating boundary which is then translated into terms of e.m.f. The behaviour thus presented is similar to that which forms the basis of 'maser' operation and, carrying the concept further on the basis of our most recent work, we believe that, by suitable selection of crystal parameters, materials and temperatures, it is possible so to adjust the resonating boundary frequency that translation from any one electromagnetic frequency into another may be possible.

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Structure of Calcium Soap Fibres

Previous publications on soap particles have contained conflicting views and evidence as to the orientation of the hydrocarbon chains within the particles. This is true even for a single soap, calcium stearate, and may be due to different methods of preparation leading to different crystal habits and/or structures.

So far as we are aware, no direct evidence from electron microscopy has yet been published concerning calcium soap fibres. We are particularly interested in materials such as are used in lubricating greases, and the samples we have examined were in fact prepared from calcium-based greases made with commercial grade fatty acid. It must be noted, therefore, that although our fibres contained a high proportion of C_{18} fatty acid, some of this was unsaturated and there were also minor proportions of acids of other chain-lengths present.

The method of sample preparation was the simple one of pressing a microscope grid coated with a carbon film on to a smear of the grease. The grid was then removed, washed in *n*-heptane to remove residual oil from the soap particles transferred, and examined in a high-resolution microscope without further treatment. Care was taken to keep the beam current low and to minimize the time of exposure of the sample to the electron beam.

Two types of soap fibre are commonly found in this type of grease: (i) small so-called 'twisted' fibres of widths about 0·06μ, which actually have more the appearance of helically rolled thin ribbons; (ii) ribbons of variable larger dimensions which have no twist.

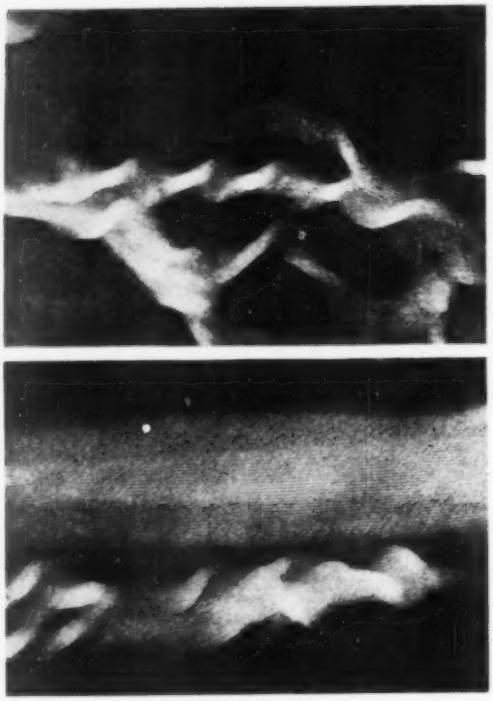

Fig. 1. Electron micrographs of calcium soap fibres showing structural detail (reverse printed for clarity). (× 114,000)

On examining both types at high resolution, striations were seen running parallel to the lengths of the fibres. The spacing of these striations is 42 Å., which, in the absence of an accurate calibration for the microscope, agrees well enough with the long-spacing value of 47·5 Å. derived from X-ray diffraction patterns of the soap. It is concluded that the striations are due to the 'edge on' view of the layers of metal atoms in the soap structure, which thus run approximately parallel to the direction of thickness and lengthwise. Fig. 1 shows the effect in both the straight and 'twisted' types of fibre, and does in fact help to suggest that there may be no marked difference in the structures of the two types. Furthermore, it gives some support for the idea sometimes entertained, that the small 'twisted' fibres result from the splitting up of the larger flat ones. In other micrographs of these grease fibres, edge dislocations have been seen, and traces of moiré fringe effects have been seen in crossed fibres.

Camp and Shuttleworth[1] found somewhat similar detail in sodium laurate fibres produced from aqueous solution, and from it they drew the same conclusions regarding the disposition of the molecules, thus supporting the ideas of Bondi and co-workers[2] on soap fibres generally. They found it necessary, however, to resort to metal shadowing in order to reveal this detail, and they believed that they were seeing agglomerates of shadowing metal nucleating on some unit within the fibre.

It seems likely that not all soaps crystallize in this way. Vold[3], using the same X-ray technique as Bondi, found sodium palmitate to fit in with the older ideas[4], namely, to have its molecular layers arranged perpendicularly to the thickness of the fibre. She claimed indirect evidence that calcium stearate, presumably the monohydrate, also obeyed the older pattern. Stanley[5] carried out some X-ray diffraction work on calcium stearate monohydrate using material re-crystallized from a mixture of propylene glycol and chloroform; and in the lath-like crystals resulting he also found evidence that this soap crystallized with its molecular layers perpendicular to the direction of thickness.

The fibres with which we are working are formed under very different conditions, and differences of habit and/or structure seem not unreasonable, particularly in view of the impure nature of our material. What is surprising is that the structural detail is more stable and visible in the instrument than might be expected from accounts of other work in electron microscopes on crystalline long-chain compounds. It has not been necessary to resort to metal shadowing as did Camp and Shuttleworth, or to use osmium tetroxide as did Trurnit and Schidlovsky[6] when studying deposited multilayers of soaps. The metal atoms in calcium stearate are, admittedly, heavier than those in sodium laurate; but they are only half as numerous, and, from simplified considerations of electron scattering power relative to carbon, they are likely to be only about 40 per cent more effective than the sodium atoms. We have noted striations still visible in these untreated calcium soap fibres after exposures of 3½ min. to the beam. The stability may in part explain the visibility.

Supposing that these grease fibres differ only from Stanley's thin crystals in external form, then their stability compared with sodium laurate could be due to a structure different from the bimolecular sheet arrangement widely accepted for soaps of monovalent metals. In his communication Stanley proposed an arrangement of overlapping molecules which might be less easily disrupted. It is noteworthy that such calcium soap fibres seldom show any longitudinal splitting of the type seen, for example, in some sodium soaps.

A comparison of X-ray long spacing values for Stanley's pure calcium stearate (50·3 Å.) and our fibres (47·5 Å.) suggests to us that the two materials may have essentially the same structure. The value for our soap is smaller by an amount roughly in keeping with the probable distribution of chain-length in our raw material. In considering the properties of these fibres we should not, however, overlook the possibility of effects introduced by minor components of the fatty acid mixture employed. Bondi, for example, reported that it was sometimes impossible to produce fibres from pure soaps.

We are continuing and extending these electron microscope investigations on soap fibres in greases, and hope to publish a fuller account in due course.

We thank the Directors of "Shell" Research, Ltd., for permission to publish this communication.

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CHEMISTRY

Deviations from the Steady-State in Ion Transfer through Perm selective Membranes

During experiments on polarization phenomena of perm-selective membranes, results were obtained which were inconsistent with the generally accepted idea that during the transfer of ions through such membranes by means of a constant direct current, a steady state is established under given experimental conditions[1].

The observation led to a series of rigidly controlled experiments in which I attempted to determine whether in fact a steady state is obtained.

A constant direct current was passed through a homogeneous cation exchange membrane bounded on both sides by 0·01 *N* silver nitrate solution. Silver electrodes were used, and the current obtained from a constant voltage rectifier (max. output : 400 V.) with less than 0·2 per cent ripple. To eliminate current variations a 44-k.ohm resistance was placed in series with the experimental cell. The potential difference through the system was measured by means of saturated calomel electrodes through 0·01 *N* potassium chloride/0·01 *N* potassium nitrate salt bridges, and a calibrated oscilloscope with d.c. amplifier. Measurements were made at various current densities and the current measured by means of an avometer. The solutions were stirred at 1,100 r.p.m. with glass stirrers.

After allowing some time for constant conditions to be established, I found that with the passage of the direct current, an unharmonic oscillation of the potential difference between the two sides of the membrane was obtained, about a constant average value. The maximum spread of the oscillation varied with the current density and at 30 m.amp./cm.^{2} increased to about 500 mV. (Table 1).

A control experiment in which the membrane was left out gave a maximum value at 30 m.amp./cm.^{2} of 20 mV. (Table 1). Further tests repeated with accumulators as the direct-current source gave similar results.

Table 1

Current density (m.amp./cm.^{2})	Spread of oscillation (mV.)		
	0·01 *N* $AgNO_3$	Control experiment	0·01 *N* $AgNO_3$ in agar–agar gel
1·5	5	5	20
3	10	5	100
6	150	10	1,000
15	300	20	8,000
30	500	20	

In order to limit all other effects except those caused by current and diffusion, an additional experiment was made in which the solution in the cell was replaced by an agar–agar gel of the same ionic concentration. In this case, the oscillation spread was much wider and gave a value of 8,000 mV. at 15 m.amp./cm.^{2} At higher current densities the overall voltage increased to such an extent that no constant current could be obtained (see Table 1).

Experiments with an anionic exchange membrane in 0·01 *N* potassium chloride gave similar results.

Since, for steady-state conditions, the potential difference between two points in the system must be constant by definition, the experiments seem to indicate that during ion transport through perm-selective membranes by means of a constant direct current, steady-state conditions need not generally appear. I feel that it is necessary, therefore, to examine anew current theories on such transfer processes, and investigations in this direction are now being undertaken.

I am indebted to Mr. Y. Mahler, of the Electronics Laboratory for his co-operation in the planning and setting up of the measurements.

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A New Calcium Magnesiosilicate

A detailed investigation is in progress of high-temperature phase equilibria in the system $2CaO.SiO_2$ – $3CaO.MgO.2SiO_2$ mainly by special methods of high-temperature microscopy[1,2] and X-ray analysis[3]. A new compound has been located of the approximate molar composition $(2CaO.SiO_2)_{5\cdot6}(3CaO.MgO.2SiO_2)_{4\cdot4}$ characterized by the X-ray diffraction pattern given in Table 1. This composition was prepared from crushed quartz (99·95 per cent pure), calcium carbonate (99·9 per cent pure), and magnesium oxide (99·9 per cent pure), by ignition at 1,250° C. in platinum boats in a platinum/rhodium resistance furnace. The fineness of the reaction mixture during ignition is of critical importance to the formation of the new compound. During a heat-treatment of 10 days duration the mixture was ground every two days to pass a 300-mesh sieve. Failure to grind to at least such fineness led to the formation of mainly $\gamma 2CaO.SiO_2$ and $3CaO.MgO.2SiO_2$ with only a small proportion of the new phase.

The X-ray powder measurements were obtained at room temperature in a Guinier-type focusing camera, 114 mm. diameter with copper-$K\alpha$ radiation. Relative intensities (I) were estimated visually on an arbitrary scale from 1 (very weak) to 10 (very strong). The density of the new compound is 3·30 and the optical properties are as follows : biaxial positive 2*V* medium (approximately 30°), RI_{Na} $\alpha = 1{\cdot}711$, $\gamma = 1{\cdot}725$.

The phase is formed by solid-state reaction and does not melt congruently.

Sharp, Johnson and Andrews[4] report a new phase, *T*, the presence of which was detected in basic arc

Table 1. Room Temperature X-Ray Powder Measurements for a New Calcium Magnesiosilicate

d	*I*	*d*	*I*	*d*	*I*	*d*	*I*
3·84	1	2·580	2	2·001	3	1·588	1
3·79	1	2·548	2	1·953	1	1·576	1
3·48	2	2·481	2	1·924	5	1·563	3
3·37	2	2·447	2	1·897	2	1·558	3
3·22	2	2·421	2	1·876	2	1·548	2
2·95	2	2·340	2	1·836	2		
2·829	4	2·292	1	1·747	1	1·428	1
2·771	1	2·228	4	1·727	1	1·420	1
2·732	10	2·210	4	1·708	1		
2·718	10	2·172	2	1·687	2	1·363	2
2·668	8	2·110	2	1·669	1	1·336	3
2·648	1	2·080	2	1·649	2	1·297	1
2·631	1	2·070	3	1·621	1	1·243	1*B*
2·594	2	2·020	1	1·606	1		

B, broad line

furnace slags. The lines in Johnson's X-ray patterns (private communication), which he considers to be due to a new phase, seem to accord with the strongest lines found in the pattern reported here. The stable phase assemblages between the new compound and adjoining compounds are being studied. It is already clear, however, that over a wide range of composition between $2CaO,SiO_2$ and $3CaO,MgO,2SiO_2$ the X-ray pattern of the new phase is unaltered, supporting the view that the phase is a singular compound and not a member of a solid-solution series.

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Use of Krypton for Surface Area Measurements

We have recently discussed[1] some criteria for the applicability of various gases in measuring the surface areas of solids by the Brunauer–Emmett–Teller[2] method. We concluded that the use of krypton in this technique led to valid and useful results and that previous criticism of the use of this gas was unfounded. However, Thomas[3] has again suggested that 'anomalous' Brunauer–Emmett–Teller plots obtained from krypton adsorption measurements render the use of this gas undesirable. He proposes that the occurrence of phase-changes in the adsorbed film, evidenced by discontinuities in the adsorption isotherm, are associated with these 'anomalous' (and presumably suspect) results.

We wish to re-emphasize the fact that an evaluation of monolayer coverage must be based on the behaviour of the adsorbed film when the first monolayer is nearly complete. Two-dimensional condensation or other transitions in the adsorbed film at lower or higher coverages do not appear to affect the validity of the surface areas evaluated from linear Brunauer–Emmett–Teller plots in the monolayer region. McDermot and Lawton[4], for example, were able to evaluate the surface area of a graphite sample from krypton-adsorption data even though they observed two discontinuities in the isotherm at 77° K. The work of Roberts[5] strongly suggests that krypton adsorbed on an evaporated iron film can be considered a two-dimensional liquid at coverages greater than about 80 per cent of the first monolayer. The energetic considerations which we have previously used[1] are therefore applicable, and valid surface area measurements are obtained in these cases.

We submit, therefore, that the non-linear parts of the plots described by Thomas are irrelevant to the purposes of surface area measurement. The application of the self-consistency criterion[1,6]:

$$p/p_0|_{v_m} = \frac{1}{1+\sqrt{c}}$$

suggests, however, that if his measurements had been carried to somewhat higher pressures, Thomas would have obtained valid v_m values.

It must be remembered that the useful linear range of a Brunauer–Emmett–Teller plot varies, in terms of relative pressure, with the nature of the solid surface, as we have already shown[1].

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Properties of Polyadenylic Acid in Methanol Solution

Until recent years, methanol and ethanol were universally regarded only as precipitants for nucleic acids. However, Geiduschek and Holtzer[1], and later Coates and Jordan[2], showed that at sufficiently low ionic strengths both the above lose their precipitating capacity for deoxyribonucleic acid (DNA) and in fact becomes fairly good solvents, depending upon the concentration of electrolyte.

The above authors have also observed a profound alteration of the over-all macromolecular properties of DNA in the above media, including a drastic fall in intrinsic viscosity and rise in frictional coefficient without any important change in molecular weight. The extensive molecular collapse indicated by the above was largely reversed on replacement of alcohol by dialysis versus water, suggesting that irreversible 'denaturation' in the classical sense had not occurred in this instance.

The present investigation deals with the properties of polyriboadenylic acid (poly A) dissolved in anhydrous methanol. Such criteria as ultra-violet hypochromism and optical rotation have been interpreted as indicating that the alkaline form of poly A in aqueous solution possesses varying degrees of helical content, depending on conditions, and displays in fact many of the characteristics of an intermittently helical system, being rather analogous to ribonucleic acid[3,4].

Solutions of poly A (1 per cent) in water were dialysed exhaustively versus anhydrous methanol according to the procedure of Geiduschek[1]. (The poly A used was prepared by the action of the polynucleotide phosphorylase of *M. lysodeikticus* (supplied by Dr. R. Beere) upon adenosine diphosphate.) After dialysis they were diluted five-fold with methanol. The final water content was less than 1 per cent. No dependence of molecular properties on water content was observed for values of the latter less than 5 per cent.

Table 1

Solvent	Water (0·001 *M* sodium acetate)	Methanol (0·001 *M* sodium acetate)
Absorbancy (λ = 260 mμ (20° C.))	9,500	13,600
Absorbancy* (λ = 260 mμ (50° C.))	12,400	13,600
Sedimentation coefficient ($S^{20}_{0,w} \times 10^{13}$)	6·9	50
Intrinsic viscosity	16·8	0·26
Optical rotation ($[\alpha]_d$)	+ 100°	− 25

* Corrected for thermal expansion of solvent.

The results (Table 1) can be summarized briefly: The high degree of dextrorotation ($[\alpha]_d$ = 100–150°) normally characteristic of the alkaline form of poly A in water[3,4] is, in methanol containing 0·001 *M* sodium acetate, replaced by a small negative rotation.

Furthermore, most of the hypochromism displayed by poly A in water disappears in methanol solution, as Table 1 shows. The absorbancy at 260 mμ increases by more than 40 per cent in the latter medium and becomes independent of temperature. Inasmuch as the absorbancy of the monomer, adenosine monophosphate, was found to be the same in water and in methanol there is a definite implication that the result with poly A reflects some modification in the secondary structure or conformation of the polymer.

The macromolecular properties of poly A underwent an equally dramatic change. A profound increase in the sedimentation coefficient and a decrease in intrinsic viscosity occur in methanol solution, as has already been observed in the case of DNA (refs. 1 and 2).

All these effects were reversible on removal of methanol by dialysis versus water.

The effect of methanol upon the over-all *macromolecular* properties of poly A is entirely in harmony with the reported results upon DNA. In both cases a dominant factor in the molecular collapse is undoubtedly the largely ion-paired character of the phosphate groups in alcoholic solution[3]. The electrostatic stress, which is important for aqueous solutions of polyelectrolytes at the low ionic strength (0·001) of these investigations, is thus largely relieved.

Thus the apparent helical content of poly A largely disappears in methanol, as judged by both the hypochromism and optical rotation criteria.

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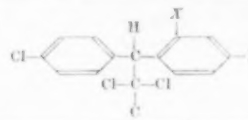
Toxicity of 2-(2-Halogen-4-Chlorophenyl)-2-(4-Chlorophenyl)-1,1,1-Trichloroethanes to Normal and to DDT-Resistant House-Flies

As part of a programme designed to test a free-radical hypothesis of insecticidal action for DDT[1], a series of new DDT compounds substituted by halogen in the ortho-position was synthesized and the toxicity to normal and to DDT-resistant house-flies (*Musca domestica* L.) was determined (Table 1). The results are of unusual significance in regard to: (1) the mechanism of DDT resistance, and (2) the relative toxicity of the positional isomers of DDT.

In the susceptible *S*-strain of the fly, a direct correlation exists between the size of the halogen in the ortho position and the LD_{50} value. A reverse correlation is evident with *in vitro* enzymatic dehydrochlorination. If this detoxication mechanism is indeed the basis for DDT-resistance in the resistant *R*-strain, the toxicity of these compounds to the tolerant strain should be the resultant of these two inverse relationships. Results support this supposition with the maximum insecticidal effectiveness occurring in the 2-(2,4-dichlorophenyl)-2-(4-chlorophenyl)-1,1,1-trichloroethane (III).

Table 1. Toxicity Spectra of DDT Analogues to Susceptible and Resistant Houseflies and Correlation with Dehydrochlorinase Activity



Compound	X	Y	LD_{50} (μgm./♀ fly) *S*-strain (CSMA)	LD_{50} (μgm./♀ fly) *R*-strain (DDT-45)	Relative enzymatic dehydrochlorination (*in vitro*) *R*-strain Brei
I	H	Cl	0·1	> 40	+ + + +
II	F	Cl	0·2	14·0	+ +
III	Cl	Cl	0·4	0·8	+
IV	Br	Cl	1·1	2·0	−
V	H	H	3·3	> 40	+ + +
VI	Cl	H	6·2	~ 30	−

LD_{50} values are averages of duplicated tests made on at least two successive generations of 5-day-old flies. Each point on dosage–mortality curve was determined by topical application (in 1 μl. acetone) to 80–100 female flies. Treated flies were held at 75–80° F. and percentage mortality recorded at 24 hr. Enzyme activity was measured on a concentrated homogenate of *R*-strain, assayed by the glass bead procedure (ref. 3).

The toxicity spectrum with the *S*-strain indicates that mono-ortho substitution by a chlorine atom reduces toxicity of the parent compound by a small factor. (Compare I with III and V with VI.) When one observes the much greater difference in toxicity between I and V and between III and VI, it becomes evident that the weak activity of VI is primarily the result of the loss of the para-substituent. Hindrance of 'free rotability' of the benzene rings[2] by a single ortho-chloro-substituent can only be of lesser importance in reducing the insecticidal properties of the molecule. The possibility that samples of VI may contain a small amount of I and thus account for the toxicity of the former compound to *S*-strains may be raised. Barring synergism, the fact that VI is still somewhat toxic to the *R*-strain would appear to preclude this possibility.

Further work is in progress to evaluate these and related compounds against different fly strains, naturally tolerant insects, and species with acquired resistance. Selection experiments are also being conducted to determine if the house fly has the capacity to develop resistance to these new compounds. Data on the methods of synthesis and characterization of these new compounds will be published elsewhere.

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MINERALOGY and GEOLOGY

Infra-red Investigation of the Migration of Lithium Ions into Empty Octahedral Sites in Muscovite and Montmorillonite

In work on the reaction of molten salts with layer-lattice silicates, it was found that molten lithium nitrate removed a large portion of the potassium from muscovite (< 5μ) and lithium was fixed in a not readily exchangeable manner[1]. It was suggested that lithium ions migrated into the vacant octahedral positions of the dioctahedral micas in a manner similar to that postulated previously by Hofmann and Klemen[2] and Greene-Kelly[3] for lithium-saturated montmorillonite on heat treatment. X-ray diffraction measurements of the 060 spacing of muscovite treated with lithium showed no significant increase, whereas an increase might be expected in conversion of a dioctahedral composition to a trioctahedral composition. Attempts to apply the infra-red technique of Serratosa and Bradley[4] for determination of the orientation of OH-bond axes to indicate formation of a trioctahedral composition were also unsuccessful.

Stubican and Roy[5] observed that an increase in the amount of magnesium in octahedral sites in a muscovite-phengite series caused the absorption band with frequency 935 cm.$^{-1}$ to become more poorly defined. They allocated this band to H–O...X^{3+} by comparison of spectra for minerals with their deuterated synthetic analogues, and showed that it moves from 935 to 910 to 827 cm.$^{-1}$ as the ions change from aluminium to gallium to iron. Serratosa[6] has assigned the 915 cm.$^{-1}$ band in montmorillonite to H–O...Al^{3+} on the basis that this band decreases in intensity at a rate concomitant with those of the stretching frequency (3,600 cm.$^{-1}$) on heating to successively increased temperatures.

The dioctahedral compositions of the muscovite and montmorillonite structures provide each structural OH with two octahedral ion neighbours, predominantly aluminium in these two minerals. The effect of heavier octahedral neighbours or a greater number of neighbours on the OH bending frequency is considerable[5,6].

If lithium ions enter the empty octahedral sites in muscovite and montmorillonite, one would expect that the three octahedral neighbours (2 Al, 1 Li) of the OH would anchor it more firmly and lower its bending frequency. Fig. 1 shows superposed absorption records of the 5–2μ fraction of (*A*) untreated muscovite (Delamica) and (*B*) the same material after treatment with molten lithium nitrate for 480 hr. The absorption feature appearing at 915 cm.$^{-1}$ in the untreated muscovite is absent after the treatment with lithium nitrate. In addition, the features at 828 cm.$^{-1}$ and 798 cm.$^{-1}$ are eliminated. Treatment of montmorillonite (Wyoming bentonite) with molten potassium nitrate at 350° C. did not affect the 915 cm.$^{-1}$ OH bending frequency, whereas treatment with molten lithium nitrate at 300° C. eliminated the band. These results give experimental verification of migration of lithium ions into empty octahedral sites in muscovite and montmorillonite as postulated previously.

A more detailed account of this work will be published elsewhere. We acknowledge helpful discussions with Dr. W. F. Bradley. The work was supported in part by a grant from the National Science Foundation (*NSF G6063*). The assistance of Dr. John Amy and Marcia Dilling, Chemistry Department, in obtaining the infra-red spectra is gratefully acknowledged.

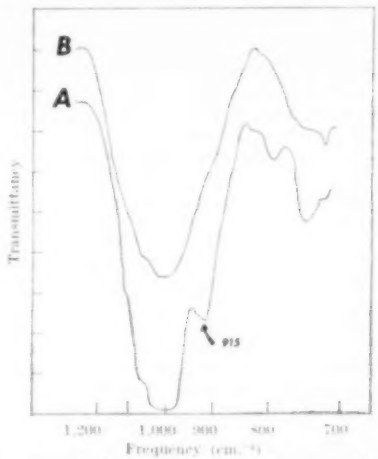

Fig. 1. Superposed infra-red spectra of muscovite (Delamica) (5 – 2μ) (*A*) untreated and (*B*) treated with molten lithium nitrate at 300° C. for 480 hr.

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Mammoths in the Cotswolds

Recent examples of fleeting opportunities provided to archæologists, geologists and others by modern methods of excavation are common knowledge; all too often an opportunity passes before advantage can be taken of it. The following notes illustrate the fruits of sustained observation on one hand, and of good fortune on the other, which we have witnessed in the past year or so.

First, pits worked over a period at Great Chessells, near Bourton-on-the-Water, Glos., in a headwater tributary of the Windrush, were watched by Mrs. Helen E. O'Neil, because she was excavating a Romano-British site progressively destroyed by exploitation. She obtained from the gravels an important collection of mammoth teeth and two molars of woolly rhinoceros[1]. They are comparable with material collected over many years from the lower gravels of the Summertown–Radley terrace of the Upper Thames and its tributaries around Oxford. The association united the deposits of the headwaters of one such tributary, namely, the Windrush, with those of its confluence with the Thames.

Further, material of the same form as these molars of mammoth was recovered recently by one of us

(L. R.) from gravels of the Severn near Worcester[2], and it is known in those of the Avon[3,4].

Within recent months, two notable and unique additions have been made, namely, a comparable molar from the Cheltenham Sands at Charlton Kings[5], and a specimen from the Paxford gravel at Ditchford, between Stretton-on-Fosse and Moreton-in-Marsh, Glos., which again we owe to Mrs. O'Neil.

The molar from Ditchford raises old issues because the succession there was studied years ago by Dr. Mabel Tomlinson[4], who concluded that the gravel lay between two glacial deposits, an older or Campden Tunnel Drift, and a younger or Moreton Drift. The pit was worked extensively for a short time, and in the autumn of 1960 it was filled in ; but the sections confirmed Dr. Tomlinson's conclusions because we saw all three deposits in continuous working-faces[6]. Although irregular surfaces occurred below and above the Paxford gravel, in some places it passed up from the underlying drift with no more than changes of constituents. At the top the distinctive Moreton Drift, with abundant flints, lay on the gravel, which was in some places strongly disturbed, and in others undisturbed. Thus, in spite of striking differences in the constituents of the three deposits, it would be hard to say that they represent events widely separated in time.

The importance of the molar from the gravel at Ditchford thus lies in the fact that it is associated stratigraphically with glacial deposits, which may be traced into the Avon valley and into the head of the Evenlode. Farther down the latter valley, in the Oxford district, is the region of abundant occurrences of teeth and bones of mammoth with an associated fauna, in the lower part of the Summertown–Radley gravels. The upper part, unconformable on the lower, contains remains of hippopotamus and other mammals, and freshwater molluscs[6].

The tributary of the Windrush mentioned above is separated from the upper reaches of the Evenlode by a ridge of Jurassic rocks near Stow-on-the-Wold.

If mammoth teeth found in the various deposits recorded in this communication may be accepted as a common and diagnostic palæontological factor, a sense of contemporaneity is introduced between gravels of the Upper Thames and its tributaries, and of the Severn and Avon, glacial deposits, and the Cheltenham Sand (which in part may be of æolian origin). In fact the molars are known widely, from the Cotswolds to the Lower Severn (for example, Barnwood) and to the Midlands, and they are distinctive: the 'Siberian' form, known also in younger deposits, sometimes occurs. Consequently, the significance of the several deposits and the tooth in the Ditchford pit, close to the divide between the Thames and Severn systems, can be readily determined, and the result is valuable in connexion with the correlation of the superficial deposits in the basins of the two rivers.

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BIOCHEMISTRY

Comparison of the β-Lactoglobulins of Buffalo's Milk and Cow's Milk

Aschaffenberg and Drewry[1,2] demonstrated by paper electrophoresis at *p*H 8·6 that β-lactoglobulins of cow's milk (sometimes described in the literature as bovine β-lactoglobulin) occurred in two different forms, β-lactoglobulin *A* and β-lactoglobulin *B*. The milk of individual animals contained either both or only one of these components, and the formation of these proteins by the mammary gland was genetically controlled. These observations led to the present work on the whey proteins of buffalo's milk, which is widely consumed in India and other eastern countries, to see whether such a possibility existed among this species of animal.

The typing procedure of Aschaffenberg and Drewry[3] was applied to individual samples of milk collected from 70 buffaloes and also to two samples of pooled milk. The animals belonged to mixed breeds with features of one or other of the common Indian buffaloes[4] relatively dominant. Paper electrophoresis experiments were carried out in barbitone buffer of *p*H 8·6 ($I = 0{\cdot}05$), applying a voltage of 240 V., by both hanging- and horizontal-strip techniques, using Whatman No. 4 filter paper. A sample of whey proteins of cow's milk containing almost equal proportions of β-lactoglobulins *A* and *B* was run as a standard for comparison with each experiment. It was found (Fig. 1) that buffalo's milk contained only one type of β-lactoglobulin which migrates to the position corresponding to the β-lactoglobulin *B* of cow's milk. In view of the fact that the same results were obtained from as many as 70 individual samples, it appears that the genetic control as reflected in the case of cow's milk, does not exist in the buffalo.

The electropherograms also reveal a distinctly different movement of the α-lactalbumin band of the buffalo's milk from that of cow's milk, the former moving ahead of the latter. This offers a possibility of developing a method, which is being explored, of detecting adulteration of one by the other.

The buffalo β-lactoglobulin crystallized in diamond shaped form and the lactalbumin in needles when the

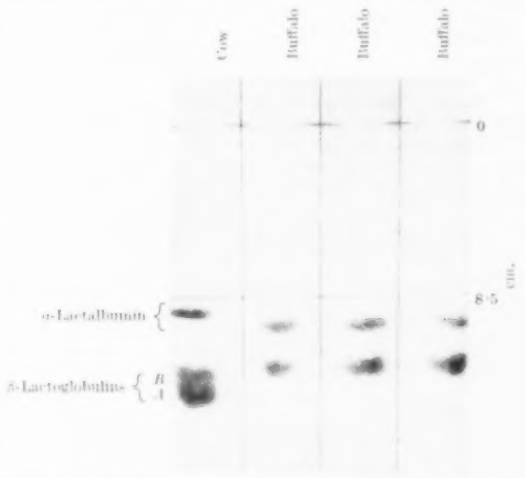

Fig. 1. Electropherogram of whey proteins of cow's and buffalo's milk (horizontal-strip technique, bromo-phenol blue staining)

method of Aschaffenberg and Drewry[3] with minor modifications was employed. Preliminary electrophoretic experiments in a Tiselius apparatus, of crystalline buffalo β-lactoglobulin, indicated its isoelectric point to be approximately 5·25 and the electrophoretic patterns obtained near the isoelectric point with acetate buffers of 0·1 ionic strength were found to be asymmetrical or partially resolved on the descending side and hypersharp on the ascending side. Sedimentation experiments with a Spinco model *E* analytical ultracentrifuge with protein concentrations up to 6·8 per cent and at 20° C. and low temperatures (about 8° C.) gave symmetrical patterns. These results show that there is close similarity between physico-chemical properties of buffalo β-lactoglobulin and β-lactoglobulin *B* of cow's milk[3,4].

Further work is in progress and details will be published elsewhere.

We are indebted to Messrs. Alpine Dairy and Farm, Agarpara, W. Bengal, and particularly to Mr. B. K. Choudhury for supplying the milk and helping in identification of individual animals.

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Intracellular Distribution of Ubiquinone in Rat Liver under Certain Stress Conditions

Observations on the effects of pantothenic acid deficiency on mitochondrial composition in relation to oxidative metabolism in rat liver were reported earlier[1]. In the present communication, observations on intracellular distribution of ubiquinone in the pantothenic acid-deficient rat liver are presented. The effects of vanadium administration and of vitamin A-deficiency have also been studied, since vanadium is known to cause decreased hepatic coenzyme *A* (ref. 2) and vitamin A-deficiency results in increased ubiquinone-level[3].

Dietary deficiencies of pantothenic acid and vitamin A were produced by feeding weanling rats (40–50 gm.), Wistar strain, a 10 per cent purified casein ration deficient in the respective vitamin and replete in all other respects, for a period of 8 weeks. To one group of rats, fed the casein ration with all the vitamins, ammonium vanadate was administered intraperitoneally (0·6 mgm./rat/week), throughout the experimental period. The animals were killed, livers quickly removed and chilled in cracked ice. Livers were homogenized in isotonic (0·25 *M*) sucrose, nuclear and mitochondrial fractions separated in a *PR*-2 International refrigerated centrifuge[4] and microsomes in a Spinco preparative centrifuge[5]. Determinations of coenzyme *A*, ubiquinone and mitochondrial succinoxidase activity were as described before[1]. The supernatant fraction was freeze-dried before saponification in the assay procedure for ubiquinone.

The results (Table 1) show normal rat liver ubiquinone to have an average distribution of 29·1 per cent in the nuclei, 37·8 per cent in the mitochondria, 14·9 per cent in the microsomes and 5·5 per cent in the supernatant fraction. Of the total coenzyme *Q*, 84–93 per cent was recovered in the various cytoplasmic fractions.

Vanadium administration, as also pantothenic acid-deficiency, result in marked and very similar decreases in total coenzyme *A*, mitochondrial ubiquinone and succinoxidase activity. This close parallelism suggests that the reduced hepatic coenzyme *A*-level is the primary cause of the decrease in ubiquinone; the involvement of coenzyme *A* in the biosynthesis of the isoprenoid side-chain of the ubiquinone molecule is known (cf. ref. 1). Vitamin A-deficiency results in elevated levels of ubiquinone in all the cell fractions, being particularly marked in the microsomal and supernatant fractions and is unattended by any change in succinoxidase activity.

Our thanks are due to the Indian Council of Medical Research, New Delhi, for a research grant.

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Table 1. Intracellular Distribution of Ubiquinone in Rat Liver

Group	Ubiquinone					Coenzyme *A* units	Succinoxidase activity (μl.oxygen/hr.)
	Whole liver (μgm.)	Nuclei (μgm.)	Mitochondria (μgm.)	Microsomes (μgm.)	Supernatant (μgm.)		
10 per cent casein	127 ± 7·6	37 ± 4·1	48 ± 2·7	19 ± 3·1	7 ± 1·6	164 ± 11	1,304 ± 32
10 per cent casein + vanadium	97 ± 9·9	33 ± 4·3	33 ± 1·9	13 ± 1·8	6 ± 0·9	89 ± 17	996 ± 51
10 per cent casein − pantothenic acid	103 ± 3·1	33 ± 5·6	36 ± 4·1	17 ± 2·4	6 ± 1·1	96 ± 6	1,031 ± 69
10 per cent casein − vitamin A	187 ± 11·6	46 ± 3·9	61 ± 6·2	34 ± 2·4	17 ± 4·1	—	1,361 ± 98

Results are averages of four independent determinations ± *S.E.*, and are expressed per gm. fresh liver weight.

Extraction of Nucleic Acid-free Lipopolysaccharides from Gram-negative Bacteria

The extraction of Gram-negative bacteria by the hot phenol method of Westphal[1] yields a lipopolysaccharide along with considerable amounts of nucleic acid. The nucleic acid can be separated from the high molecular weight lipopolysaccharide by high-speed centrifugation, but to reduce the nucleic acid to a level of less than 2 per cent may require four or five sedimentations.

It is known that when the trichloracetic acid method of Boivin is used to extract the somatic antigen, a considerable amount of the antigen may remain in the residue[2]. Working with a *Pseudomonas* species, we have found that the residue left after the dried cells have been treated with trichloracetic acid, can be extracted with phenol to yield a lipopolysaccharide virtually free from nucleic acid.

10 gm. of the acetone-dried cells were mixed for 3 hr. in 100 ml. of 0·25 *N* trichloracetic acid at a temperature of 2–4° and then centrifuged. The deposit was washed with 100 ml. of distilled water and again centrifuged. This deposit was then extracted with 45 per cent phenol at a temperature of 65–67° and, after cooling, the aqueous phase was separated, dialysed, centrifuged at 4,000 r.p.m. for 10 min. to remove debris, and the supernatant was then freeze dried. The yield of extracted material from different batches was between 300 and 400 mgm. This compares favourably with the yield of lipopolysaccharide obtained after removal of the nucleic acid by high-speed centrifugation.

The lipopolysaccharide obtained by this method contained no detectable amounts of nucleic acid and was highly pyrogenic in rabbits in doses of 0·01 µgm./kgm. body-weight. Preliminary analysis showed the presence of galactose and glucose and 45–50 per cent of a lipid soluble in chloroform.

Similar results have been obtained with *E. coli* 0111 (supplied by Dr. O. Lüderitz) and with *P. vulgaris*. In both cases the modified extraction procedure yielded highly pyrogenic, nucleic acid-free lipopolysaccharides in amounts equivalent to 2–3 per cent of the dry weight of the bacteria.

The results with these three organisms suggest that pre-treatment with trichloracetic acid before phenol extraction may be a general method of obtaining nucleic acid-free lipopolysaccharides without the lengthy procedure of high-speed centrifugation. This suggestion is supported by unpublished observations made by D. A. L. Davies (personal communication) working with different bacteria.

One of us (G. J. O'N.) acknowledges the award of a Cross Trust research scholarship during the tenure of which this work was done.

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Enzymatic Reduction of Diphosphopyridine Nucleotide with Urea

In investigating the properties of an enzymatic cycle between ammonia and nitrate[1], we have now observed the enzymatic reduction of diphosphopyridine nucleotide with urea.

The enzyme solution was prepared daily from acetone precipitates of fresh fowl liver according to the procedure already described[1]. To measure the activity, 1 ml. of 0·025 per cent solution of diphosphopyridine nucleotide was mixed with 1 ml. of enzyme solution, 1 ml. of 0·001 *M* urea solution and 0·5 ml. of

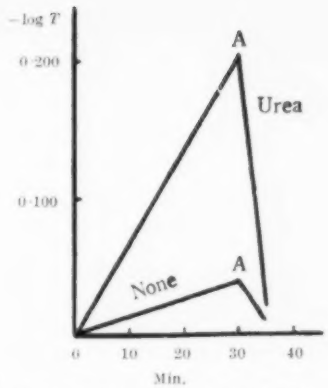

Fig. 1. Reduction of diphosphopyridine nucleotide with urea. At point *A*, alcohol dehydrogenase and acetaldehyde were added

0·2 *M tris* buffer of *p*H 7·5. Then, the increase (+) in absorption ($-\log T$) at 340 mµ was determined by a spectrophotometer at 30° C. after 30 min. As shown in Fig 1, $-\log T$ increased in the presence of urea, and a slight increase was observed in the control which contains no urea. This value must therefore be subtracted from those in tests. In the reaction mixture without enzyme, there was no change in $-\log T$. The increase of $-\log T$ was rapidly reduced when alcohol dehydrogenase and acetaldehyde were added.

The reduction does not proceed in a mixture containing phosphate buffer. The enzyme exhibits its highest activity at 35° C. and *p*H 7·5; it is activated by heating at 35–40° C. for 5 min. but destroyed at 60° C. Diphosphopyridine nucleotide is reduced with biuret or monomethylurea too, although at a slower rate than with urea.

However, it is thought that the enzymatic reduction of diphosphopyridine nucleotide may be attributed to ammonia produced from urea by the action of urease, since the nucleotide is reduced by the same enzyme solution in the presence of ammonium salts. Therefore, the formation of reduced diphosphopyridine was examined comparatively with urea and ammonium sulphate, although distinct formation of ammonia from urea by the enzyme solution employed was not established.

Table 1 shows that triphosphopyridine nucleotide can also be reduced by urea, whereas only the diphosphopyridine nucleotide is reduced with ammonia.

Table 1. Reduction of Di- and Tri-phosphopyridine Nucleotide

Nucleotide	DPN			TPN		
Substrate	Urea	Ammonia	None	Urea	Ammonia	None
$-\log T$	+0·113	+0·140	+0·025	+0·068	+0·009	+0·009

Reduction of diphosphopyridine nucleotide with ammonia accompanies the formation of its oxidation products, hydroxylamine, nitrite and nitrate. On the other hand, as illustrated from Table 2, these substances could not be demonstrated in the case of urea.

Table 2. Formation of Hydroxylamine, Nitrite and Nitrate in the Reaction Mixture

Product		Hydroxylamine	Nitrite	Nitrate
Substrate	Urea	0	0	0
	Ammonia	4×10^{-4} *M*	4×10^{-4} *M*	1×10^{-4} *M*

Further work showed that there are some other differences between the reduction of diphosphopyridine nucleotide with urea and that with ammonia, especially in connexion with the re-oxidation of the reduced nucleotide formed by nitrate reductase in the reaction mixture, substrate inhibition, optimum temperature and purification of enzyme.

On the basis of this work, the reduction of diphosphopyridine nucleotide with urea may be an enzymatic electron transfer from urea to the nucleotide, and not from ammonia in association with urease and ammonium dehydrogenase. In other words, the reaction appears to be an enzymatic dehydrogenation of urea which serves as an electron donor. This reaction has not previously been observed so far as we know. However, it should not be called urea dehydrogenase, until the dehydrogenation products of urea are established and the reaction mechanism is explained. Work is in progress to do this.

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A D-Lactic Dehydrogenase from *Leuconostoc mesenteroides*

The properties of the L-lactic dehydrogenases (L-LDH) from muscle[1-3] and yeast[4-6] have been studied extensively. Recently, the presence of lactic dehydrogenases was reported in animal tissues[7], yeast[8-10] and bacteria[11-13], specific for the D-isomer of lactic acid. The present communication describes the isolation, partial purification and some properties of a D-lactic dehydrogenase (D-LDH) from *Leuconostoc mesenteroides*.

L. mesenteroides strain No. 8042 was grown without shaking on a protease peptone medium, containing 1 per cent glucose. The cells were collected after 24 hr. growth and disintegrated sonically. The sonicate was centrifuged at 105,000*g* for 2 hr. The supernatant extract contains D- and L-LDH activity in a ratio of 20 : 1. This ratio could be increased to more than 200 : 1 by fractionation with ammonium sulphate, using the fraction precipitating between 0·15 and 0·40 saturation. At the same time the specific activity towards D-lactate was increased threefold. In the experiments described here, this partially purified preparation was used.

Dehydrogenase activity was assayed by the reduction of 2,6-dichlorophenol-indophenol (DCPIP) (1×10^{-4} *M*), measured by the decrease of optical density at 620 mμ. The assay was carried out in phosphate buffer (0·25 *M*) at *p*H 6·5, which was found to be the optimum under aerobic conditions. The enzyme preparation contained approx. 5 mgm. protein/ml. The K_m with regard to D-lactate was found to be $1{\cdot}5 \times 10^{-2}$ *M*. In the following experiments a 2×10^{-2} *M* substrate concentration was used.

In contrast to yeast LDH[1,2], neither ferricyanide nor cytochrome *c* nor molecular oxygen could replace DCPIP as hydrogen acceptor. Added di- or triphosphopyridine nucleotide (DPN, TPN) at a concentration of 2×10^{-3} *M* had no effect on the rate of reduction of DCPIP. Moreover, DPN did not serve as a hydrogen acceptor for D-lactate, nor could DPNH pass on its hydrogen atoms to pyruvate. Flavin adenine dinucleotide or flavin mononucleotide had no effect on the system.

Table 1. Substrates and Inhibitors of D-LDH from *L. mesenteroides*

Substrates	Relative velocity	Inhibitors	I_{50} (*M*)
D-Lactate	1·00	pyruvate	0·05
L-Lactate	0·005	fluoropyruvate	0·001‡
DL-Fluorolactate*	0·15	oxalate	0·0005
DL-Chlorolactate	0·03	copper†	0·0001
DL-α-Hydroxybutyrate	0·01	mercury†	0·00005
DL-glycerate	0·01		

* In presence of 0·01 *M* hydrogen cyanide; without hydrogen cyanide the enzyme was rapidly inactivated.
† After 15 min. pre-incubation with the enzyme.
‡ Calculated from activity of DL-fluorolactate without hydrogen cyanide.

Table 1 shows the substrate specificity and the effect of inhibitors. It can be seen that the substitution at the β-carbon sharply decreases the activity, in contrast to the yeast enzyme[6] and more resembling the muscle enzyme[1]. Other α- and β-hydroxy acids were not attacked, nor were glycolic acid and the ethyl ester and amide of *d,l*-lactic acid.

The enzyme differs from the flavoprotein yeast LDH in the lack of inhibition by atebrin[4] and *d,l*-mandelic acid[6]. In contrast to muscle L-LDH, *p*-chloromercuribenzoate (2×10^{-4} *M*) and iodoacetate (1×10^{-2} *M*) were without effect. Strong inhibition was caused by oxalate. Fluorolactate inhibited strongly in the absence of hydrocyanic acid, while it acted as a substrate in its presence. Moreover, fluoropyruvate did not inhibit the enzyme. This finding indicates that the product formed as a result of the dehydrogenation of fluorolactate is not identical with the synthetic product. Differences in inhibitory activity between various forms of fluoropyruvate have been described already by Busch and Nair[14]. Zinc, molybdenum, nickel, manganese, cobalt and iron (all at 1×10^{-3} *M*) did not affect enzyme activity, but copper and mercury were strong inhibitors, their effect being reversed not only by cysteine, but also by histidine, both of them at a tenfold excess over the metal ion concentration.

The *Leuconostoc mesenteroides* D-LDH resembles some of the bacterial D-LDH's described[9-11]. However, it is most closely related to that of Molinari and Lara[12] in *Propionibacterium pentosaceum* but differs from the latter in not being inhibited by atebrin and SH-agents. In the enzyme described in this communication the nature of the active site is not clear.

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Stimulation of Active Transport of Sodium from Sodium-rich Frog Muscle by Insulin and Lactate

ACTIVE excretion of sodium from muscle was first shown for cat muscle *in vivo* by Conway and Hingerty[1], and for isolated frog muscle by Desmedt[2] and by Conway *et al.*[3]. The latter workers found that when the sodium-level of muscle fibres was increased to about 60 mM/l. fibre water, by overnight immersion in cold potassium-free Ringer–Conway fluid containing 120 mM/l. sodium, it was necessary to reduce the external sodium in the presence of 10 mM/l. potassium chloride before active extrusion of sodium would occur.

The concept of a critical energy barrier to extrusion of sodium was introduced by Conway[4,5] to explain the necessity of reducing the external sodium, or of increasing the external potassium concentration above its normal level in plasma for excretion of sodium to occur. The energy barrier takes account of the electrical and osmotic gradients against which the sodium is extruded and is expressed by the relation:

$$dG/dn = RT.\ln [Na]_o/[Na]_i + E_m F \qquad (1)$$

where dG/dn is the free energy change per equivalent of sodium extruded, E_m the mean membrane potential of the muscle fibres (outside minus inside) in the recovery fluid, measured by the micro-electrode technique[6], and $[Na]_o$ and $[Na]_i$ the sodium concentrations in the recovery fluid and fibres respectively. In previous experiments[5], it was found that under the conditions used, sodium could not be extruded against a barrier greater than 2,000 cal., but it could be extruded if the barrier was reduced by lowering Na_o or by increasing K_o, and thereby reducing E_m.

In the presence of 30 units of insulin and 1 mM lactate per litre recovery fluid, I found that with muscles loaded with sodium as described above, the extrusion of sodium would occur, and at the normal plasma potassium-level of 2·5 mM/l. against an external sodium concentration of 120 mM/l. (see Table 1). At the same time about 30 mM potassium was gained by the muscles. It was found that the energy barrier against which sodium was extruded was 2,500 cal. at time of re-immersion in recovery fluid, rising to about 3,000 cal., after 3 hr., as extrusion reached completion. The mean membrane potential was 96 ± 0·9 mV. on re-immersion falling to 90 ± 1·9 mV. towards the end. The energy barrier here was closer to that computed for the intact animal[5], namely, 4,000 cal.

Examining the chloride movement under the conditions of previous experiments[5], I found that during immersion in potassium-free Ringer fluid the muscles gained an average of 20 mM chloride per litre fibre water, and that this chloride remained in the fibres even when the sodium had been extruded in exchange for potassium. However, addition of insulin and lactate to the recovery fluid produced a marked decrease in the fibre chloride.

The effect of some inhibitors on the extrusion of sodium under these conditions is summarized in Table 1.

It would appear from these experiments that the fall of the critical energy-level of extrusion of sodium from isolated muscle is related to a fall in the maximum electro-chemical potential at which the sodium pump can excrete sodium ions. In the light of these observations, and those of Manery *et al.*[7,8] it seems possible that insulin and lactate may play a part in the extrusion of sodium from frog muscle *in vivo*. They may also be the active constituents of plasma, which prevent the loss of potassium from isolated frog muscle[9], and maintain the membrane potential of the muscle at a higher value than found using Ringer fluid as immersion fluid[10]. In this connexion it may be of interest to note that Zierler[11] has reported that insulin increases the membrane potential of isolated muscle of rat.

Table 1. FROG SARTORII SOAKED OVERNIGHT AT 0° C. IN POTASSIUM-FREE RINGER FLUID CONTAINING 120 mM SODIUM, THEN RE-IMMERSED FOR 3 HR. AT ROOM TEMPERATURE (18° C.) IN FLUID CONTAINING 120 mM SODIUM, 2·5 mM POTASSIUM, 1 mM LACTATE AND 30 UNITS OF INSULIN PER LITRE

(Mean value after first immersion = 60·6 ± 4·2 mM/l. fibre water)

Inhibitor used	Sodium concentration in muscle (mM/l. fibre water)	
	Control	Inhibited
Ouabain (10^{-8} M/l.)	25·4 ± 1·4	46·1 ± 1·8 (11)
Iodoacetate (2 mM/l.)	23·2 ± 2·5	65·8 ± 3·6 (14)

Companion muscles were used. No. of experiments shown in brackets.

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PHYSIOLOGY

Urocanicacidurea associated with Hepatic Coma

WHILE studying the urinary chromatographic pattern of a patient in hepatic coma the presence of an abnormal spot R_F 0·14 and 0·54 in propanol/ammonia, 7 : 3, and butanol/acetic acid/water, 4 : 1 : 5, respectively, was noted after spraying paper chromatograms with diazotized *p*-sulphanilic acid. This colour reaction suggested that it might be an imidazole derivative, yet chromatography excluded the possibility of it being histamine, histidine or 1-methyl-imidazole-4-acetic acid (Table 1). As the presence of this unknown compound could not be related to the diet, or therapy, of the patient and appeared to be associated with the disease, an attempt was made to isolate it.

A 24-hr. urine sample was concentrated and acetone-precipitated according to the method of McIsaac and Page[1]. The final concentrate was streaked on Whatman No. 1 paper and chromatographed in butanol/acetic acid/water, 4 : 1 : 5. The corresponding transverse strips of paper with R_F 0·5–0·6 were eluted with ethanol. The eluates were pooled and evaporated to dryness to yield 15 mgm. of crystalline material. Recrystallization from water yielded 10·6 mgm. of chromatographically pure white crystals of urocanic acid (imidazole acrylic acid), m.p. 229° C., mixed m.p. 228–29° C., $\lambda_{max.}$ 277 mμ (pH 7·4)[2] (found : C, 40·9 ; H, 5·9 ; N, 16·0 per cent ;

Table 1

	Colour of spots on paper with			R_F values in solvent	
	Ninhydrin	Diazo-*p*-sulphanilic acid	Methyl red	*A*	*B*
Histamine	None	Red	—	0·46	0·20
Histidine	Blue	Red	—	0·15	0·10
Methylimidazole acetic acid	None	None	Pink	0·29	0·21
Imidazole acrylic acid (Urocanic acid)	None	Orange	Pink	0·14	0·54
Isolated compound	None	Orange	Pink	0·14	0·54

R_F values and colour reactions of compounds used. Solvent systems used were: *A*, propan-1-ol/ammonia, 7 : 3 and *B*, *n*-butanol/acetic acid/water, 4 : 1 : 5.

$C_6H_6O_2N_2.2H_2O$ requires C, 41·4; H, 5·8; N, 16·0 per cent).

Urocanic acid, an intermediary breakdown product in the metabolism of histidine to glutamic acid, is not normally excreted in the urine, and has only been observed after animals have been given large doses of histidine[3]. The present finding of an abnormally large amount of urocanic acid in the urine of a patient with hepatic necrosis would indicate that the pathological lesion was associated with a biochemical lesion of the enzyme system urocanase. The failure of the metabolic degradation of urocanic acid in the liver parenchyma might well have caused a deficiency of the ammonia-detoxifying glutamic acid which in part may have been responsible for the high blood ammonia-levels observed in this case.

A detailed case-history of this patient will be reported elsewhere.

We are indebted to Mrs. Pamela Taylor who did the isolation work, and we wish to thank Dr. R. W. Schayer, of the Merck Institute for Therapeutic Research, for supplying us with 1-methylimidazole-4-acetic acid.

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Effect of Chronic High and Low Salt Intakes on Adrenocortical Function

We have presented evidence which suggests that a high salt intake may be related to the development of human essential hypertension[1], and that a prolonged low salt intake is compatible with apparently normal adrenocortical function[2].

Reference[1a,2] was made to observations by others which had been interpreted to indicate that a low salt diet could be harmful by causing hypofunction of the adrenal cortex with the organism thereby rendered less responsive to stress. Such inferences were in sharp contrast to our own experience with more than 125 persons whose daily salt intake was known to have been restricted to levels ranging from 30 to 375 mgm. for periods up to 5 years[2].

In one of the reports[2] adrenocortical function appeared to be within normal limits in 3 individuals who had been maintained on daily intakes of 250–375 mgm. salt for periods of from 1 to almost 5 years. Nevertheless, since no evaluation had been made prior to salt restriction a subtle decline in adrenocortical responsiveness might have remained undetected.

Recently it became possible to re-evaluate adrenocortical activity (as this is indicated by the response to the 48-hr. adrenocorticotrophic hormone infusion test of Jenkins *et al.*[4]) in two of these same individuals when salt intake was resumed after 23 and 35 months of drastic salt restriction, respectively. The two ambulatory patients were White bachelors aged forty-nine and fifty-one years on admission. They had uncomplicated essential hypertension, and were capable of long walks on the Laboratory site daily. All menus were calculated by a dietitian, and the food was prepared and weighed in a diet kitchen. Both men were required to eat all and only the food provided. When salt was added to the regimen it was given as enteric-coated tablets under observation. Continuous 24-hr. urine collections for sodium content indicated compliance with the prescribed diet. Over a period of four months gradual increments of salt were made until during the 3 weeks preceding, and at the time of, the present work each patient was eating 40 gm. of sodium chloride daily. This is a very high salt intake by American standards[5], but these men had no symptoms from it. However, their blood pressures, which had dropped markedly on salt restriction, rose significantly on addition of salt.

Table 1 summarizes the present findings, and compares them with the results of this same test performed at various intervals during the period of salt restriction. It will be seen that the fall in total circulating eosinophiles following the infusion of adrenocorticotrophic hormone on each of days 3 and 4 was similar in these subjects whether they were off or on salt. By contrast, the urinary excretion of 17-ketosteroids and 17-hydroxycorticoids appeared to be somewhat decreased on the high salt intake. This was manifested both by smaller quantities of steroid excreted and by a response which was delayed until after the second infusion of adrenocorticotrophic hormone.

Table 1. 48-hr. Adrenocorticotrophic Hormone Test for Adrenocortical Reserve Function

Months off (−) or on (+) salt			N.S. ♂ 51 years		R.B. ♂ 49 years			
			− 12	+ 4	− 13	− 18	− 25	+ 4
Eosinophiles, mm.³ (Normal 100–250)	Day 1	Control	181	141	197	413	500	347
	,, 2	,,	166	97	206	460	369	410
	,, 3	Test	19	0	14	25	25	13
	,, 4	,,	3	0	2	38	13	10
Urinary 17-ketosteroids, mgm./24 hr. (normal: ♀ 5–15, ♂ 10–20)	Day 1	Control	13·0	7·9	10·4	10·0	12·7	13·3
	,, 2	,,	14·5	8·9	13·4	8·2	13·6	8·1
	,, 3	Test	21·1	9·7	13·2	14·5	20·5	8·2
	,, 4	,,	23·8	10·1	27·3	28·9	27·6	11·3
Urinary 17-hydroxycorticoids, mgm./24 hr. (normal: ♀ and ♂ 4–11)	Day 1	Control	9·0	8·2	4·7	7·6	7·5	9·1
	,, 2	,,	7·1	3·4	4·0	7·2	8·1	6·3
	,, 3	Test	37·6	5·9	13·1	35·3	32·6	7·7
	,, 4	,,	49·9	27·8	13·9	48·9	50·8	17·1

25 units of adrenocorticotrophic hormone infused over an 8-hr. period on each of days 3 and 4.

It would be premature to interpret the present studies as indicating that a high salt diet can impair adrenocortical function. The prompt, marked fall in total circulating eosinophiles when these patients were on the high salt intake is highly suggestive of a normally functioning adrenal cortex. Furthermore, evaluation of adrenocortical steroid production by means of urinary steroid excretion must always be suspect. Nevertheless, the results clearly indicate that by this method of estimating adrenocortical responsiveness, a high salt diet is not beneficial and a low salt diet is not harmful.

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Hypothalamic Control of Lactogenic Function in the Cat

While it is generally accepted that the hypothalamus controls the systemic release of anterior pituitary prolactin, it still remains to be established where in the hypothalamus the regulatory centres are located and how they mediate their influence.

The present investigation involves the use of a comparatively simple and effective technique which has facilitated systematic study of this problem without the use of drugs, hormones, or pituitary transplantation. It is the result of an incidental observation made by one of us (A. B. R.) that transverse section of the anterior tuber cinereum in the cat resulted in mammary growth and lactation.

A total of ten animals was used, four of which served as controls. In the six experimental cats, the diencephalic floor was aseptically exposed through the transbuccal route under barbiturate anæsthesia and the tuber cinereum sectioned transversely just behind the optic chiasm, so as not to impair the hypophyseal blood supply by injuring the median eminence or portal vessels. In three control animals the similarly exposed tuber cinereum was perforated in the midline by a stab with a large bore (No. 18) hypodermic needle, while in the fourth cat the hypothalamic section was carried out posteriorly, behind the median eminence in the premamillary region. Each operation included the removal of a mammary gland for histological examination and comparison with subsequent mammary biopsy specimens.

Because milk secretion can be induced with prolactin only in cats with fully developed ductal and lobulo-alveolar systems, positive findings can only be obtained in post-partum cats or in cats primed with ovarian hormones. The investigation reported here was confined to post-partum cats the mammary glands of which were allowed to regress over a period of up to two months.

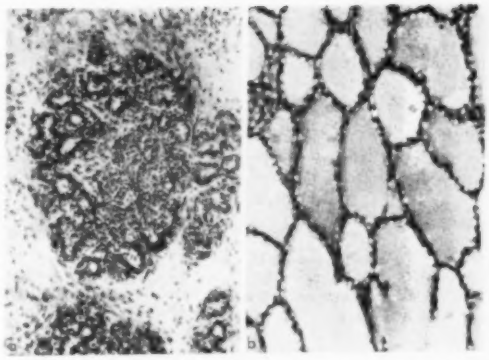

Fig. 1. Photomicrographs of mammary glands showing (*a*) preoperative resting state and (*b*) active secretory state of mammary gland in the same cat 14 days after anterior tuberal section

At the time of the operation, all the mammary glands were flat to inspection and no underlying mammary tissue could be palpated. Within three to twelve days after the tuber cinereum transection all six experimental cats, but none of the controls, showed the onset of mammary growth, which within another few days culminated in mammary hypertrophy and milk secretion indistinguishable from that seen during normal lactation (see Fig. 1).

The diabetes insipidus which often ensued at about the same time bore a variable relationship to these changes: mammary hypertrophy was observed both before and after the onset of the 'normal interphase' which accompanies the release of neurohypophyseal hormones from the degenerating posterior lobe. After a few weeks, a progressive decline in the mammary hypertrophy ensued in all but the one cat from which milk was actively withdrawn under administration of oxytocin. In this case, the involutional process was interrupted by a brief period of renewed growth.

The initiation of the observed mammary changes is known to require stimulation by prolactin. Since in these experiments the discharge of this hormone from the adenohypophysis resulted from the separation of the median eminence and hypophysis from their neural connexions with the anterior hypothalamus, the findings are explained tentatively as due to the removal of anterior hypothalamic inhibition, with or without additional facilitation through the intact posterior and lateral hypothalamic–hypophyseal pathways.

It is of interest to note that in the rabbit a centre inhibiting release of prolactin appears to be located in hypothalamic regions caudal rather than rostral to the hypophysis[1], and in an area of the hypothalamus which appears closely related to the centre controlling œstrus behaviour activated by œstrogen[2]. Since in the cat a corresponding centre controlling œstrus behaviour has been described in the anterior hypothalamus[2], which from this work appears to be the centre inhibiting release of prolactin, it is possible that these lactation-inhibiting regions of the hypothalamus may be topologically associated with the regional hypothalamic control centres sub-serving more complex and purposive patterns of behaviour such as mating and the care of the young. The latter is supported by observations that administration of prolactin to females of some species evokes maternal behaviour[3].

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Release of 5-Hydroxytryptamine from Rat Mast Cells *in vitro*

HISTAMINE is released from mast cells following the injection into animals of histamine liberators. Coincident with the release of histamine other substances have been detected in the plasma capable of causing a slow contraction of isolated smooth muscle[1-4]. Paton[4] was able to demonstrate the presence of a 'slow-contracting' substance in addition to histamine in the plasma of cats and dogs following an intravenous injection of the potent histamine release agent, compound 48/80. Preliminary experiments have shown that a similar substance appears in plasma collected from rats 5 min. after an intravenous injection of compound 48/80 (1 mgm./kgm.). The origin of the slow-contracting substance in rat plasma was investigated by means of an *in vitro* system consisting of a solution of compound 48/80, rat plasma, mast cells from the peritoneal cavity of the rat, and an isolated rat uterus preparation.

Mast cells were obtained from the rat by a method previously described[5]. The rat uterus preparation was set up according to the method of Sollero *et al.*[6]. Compound 48/80 was dissolved in physiological saline solution to a strength of 10 μgm./ml. Blood was collected from the jugular vein of rats into a syringe containing heparin (5 units/ml. blood). The blood was transferred to a centrifuge tube and plasma free of platelets obtained by centrifugation. All glassware, including syringes and the organ bath, were siliconed with 'Dri-Film' (General Electric Co.) before use.

A mixture was prepared consisting of 0·1 ml. each of the solution of compound 48/80, fresh heparinized plasma and mast cell suspension (containing approximately 1 million mast cells per ml.). When added to the organ bath the mixture was found to cause a contraction of the rat uterus. A similar contraction was produced in the absence of plasma when 0·2 ml. of a mixture consisting of 0·1 ml. vol. of compound 48/80 solution and mast cell suspension was added. 0·1 ml. of the solution of compound 48/80 alone, or when mixed with an equal volume of plasma and added to the bath, failed to stimulate the rat uterus. Similarly intact mast cells alone or with an equal volume of plasma did not cause a contraction of the isolated uterus. Prior treatment of the isolated uterus for 5 min. with dibenamine (1 μgm./ml.), 2-brom-D-lysergic acid diethylamide, known as BOL 148 (1 μgm./ml.), 1-methyl-D-lysergic acid butanolamide, known as UML 491 (0·2 μgm./ml.), or excess 48/80 (1 mgm./ml.) was found to prevent a contraction of the uterus on the addition to the bath of the mixture containing compound 48/80 and mast cells. These substances are known to inhibit the action of 5-hydroxytryptamine but are not specific. No response of the treated uterus was obtained on the addition to the bath of plasma obtained from rats 5 min. after an intravenous injection of compound 48/80.

This work suggests that a substance capable of causing a contraction of the isolated rat uterus is released from mast cells disrupted by compound 48/80. Histamine is found in mast cells in a concentration of 40 μgm. per million cells, but it does not cause contraction of the rat uterus. The 5-hydroxytryptamine concentration in rat mast cells is approximately 1/20 the concentration of histamine[7]. 5-Hydroxytryptamine was added to the bath in amounts equivalent to the calculated 5-hydroxytryptamine content of 0·1 ml. of the mast cell suspensions, and the resulting uterine contraction was similar to that produced by the mixture containing 0·1 ml. of mast cells and 0·1 ml. of compound 48/80.

The smooth muscle stimulant was released also from mast cells disrupted by a number of procedures shown previously to cause the release of histamine from mast cells[5,8-10] including (*a*) mechanical disruption; (*b*) distilled water; (*c*) an extract obtained from rat splenic tissue; (*d*) dextran, when added to serum obtained from rats following adrenalectomy; (*e*) addition of human red cells to fresh rat antiserum at 37° C. and *p*H 7. In experiments (*d*) and (*e*) with rat serum it was necessary first to decrease 5-hydroxytryptamine content of the serum by an intraperitoneal injection of reserpine (5 mgm./kgm.) at least 8 hr. before collection of the blood.

It may be concluded that 5-hydroxytryptamine or a similar substance is released together with histamine when rat mast cells are disrupted *in vitro*. It seems likely that this substance is the 'slow-contracting' substance found in rat plasma following the intravenous injection of compound 48/80.

Compound 48/80 used in these experiments was kindly supplied by Burroughs Wellcome (Australia), Ltd., reserpine by Parke Davis and Company, and BOL 148 and UML 491 by Sandoz Australia Pty., Ltd.

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Interaction of Acetylcholine, Calcium and Depolarization in the Contraction of Smooth Muscle

SMOOTH muscle which has been depolarized by external application of potassium still contracts in response to acetylcholine[1]. This response requires calcium (ref. 2, and personal communication from D. H. Jenkinson). Calcium ions alone cause the depolarized smooth muscle to contract. If an isolated

rat uterus is immersed at room temperature in calcium-free isotonic potassium sulphate–Ringer (22·0 gm. K_2SO_4, 0·36 gm. $KHCO_3$, 1·0 gm. glucose/litre) it contracts briefly and then relaxes completely. At this stage the application of very low concentrations of calcium (0·1 m*M*) causes the development of a reversible tension. The magnitude of the tension increases with concentration of calcium up to about 1·2 m*M*. Higher concentrations of calcium produce diminishing responses in tension. The maximum tensions developed by calcium are less than the maximum of which the preparation is capable, and they can be increased by acetylcholine. The effect of 10^{-5} acetylcholine added to 2·4 m*M* calcium is shown in Fig. 1.

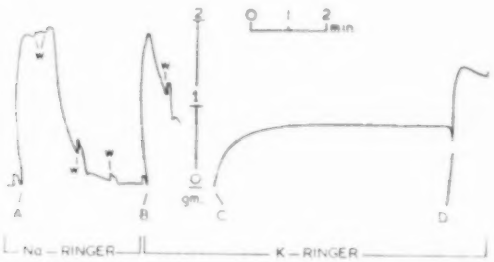

Fig. 1. Effect of acetylcholine superimposed on a maximal calcium contraction in depolarized rat uterus at 24° C. Record of isometric tension: *A*, 10^{-5} (gm./ml.) acetylcholine in sodium–Ringer solution; *B*, depolarization by calcium-free potassium sulphate–Ringer solution; contraction followed by complete relaxation; *C*, 2·4 m*M* calcium chloride; *D*, 2·4 m*M* calcium chloride + 10^{-5} acetylcholine. Between *B* and *C*, 105 min. *W*, washing

The findings that the effects of acetylcholine in depolarized smooth muscle require calcium ions, that calcium ions contract the depolarized muscle and that acetylcholine increases the uptake of calcium ions by smooth muscle[2] make it tempting to assume that the contractions produced by acetylcholine are due to an increase in uptake of calcium; but the above experiment showing that tensions due to acetylcholine can exceed those obtainable by calcium ions alone, makes it difficult to accept this simple explanation. Nevertheless, it is conceivable that acetylcholine may affect the movement of calcium at a functional site in a manner which cannot be reproduced by the external application of calcium ions.

It has been shown for heart[3] and striated muscle[4] that depolarization contractions produced by potassium ions require calcium. This also applies to smooth muscle. When rat uterus is immersed in calcium-free sodium–Ringer and depolarization contractions are elicited intermittently by immersion of the preparation in isotonic potassium sulphate–Ringer solution, the responses decline progressively and eventually disappear. At the same time the acetylcholine contractions in sodium–Ringer solution also diminish; but their decline is slower, so that a stage is reached in which depolarization contractions are abolished while considerable acetylcholine contractions are still obtainable (Fig. 2). The effects of lack of calcium are readily reversible on addition of calcium. This experiment provides new evidence that acetylcholine can cause contractions of smooth muscle which are not mediated by depolarization.

It has been previously shown that maximal doses of acetylcholine produce less tension in depolarized than in polarized smooth muscle[1]. This raises the

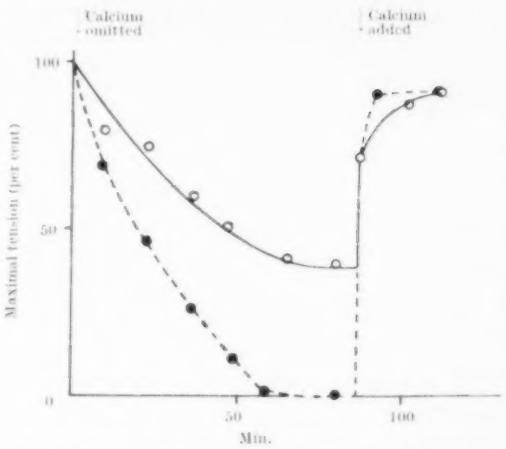

Fig. 2. Differential decline of isometric tensions produced by 10^{-4} acetylcholine (○) in sodium-Ringer solution and depolarization (immersion in isotonic potassium–Ringer solution, ●) after omission of calcium. Each point is the mean of two responses obtained from the two horns of a rat uterus, the lumens of which were opened by a longitudinal section giving sheets of approximately 1 mm. thickness. Temperature, 23° C.

question whether acetylcholine acts by the same mechanism in the two cases. In both instances the effects are antagonized by small concentrations of atropine, which seems to suggest that the receptors involved are similar. Part of the increased tension developed in polarized preparations is probably due to the occurrence of conducted impulses which are abolished after depolarization. Spike discharges in smooth muscle are increased in number by acetylcholine[5], suggesting that conducted impulses may be increased.

It appears, however, that an additional factor is involved in the greater development of tension of polarized preparations, as may be inferred from the record shown in Fig. 3. A rat uterus horn was immersed first in calcium-containing Tyrode solution and then successively in the following calcium-free solutions: potassium–Ringer, sodium–Ringer and again potassium–Ringer. Taking into account the progressive decline due to lack of calcium, it is seen that

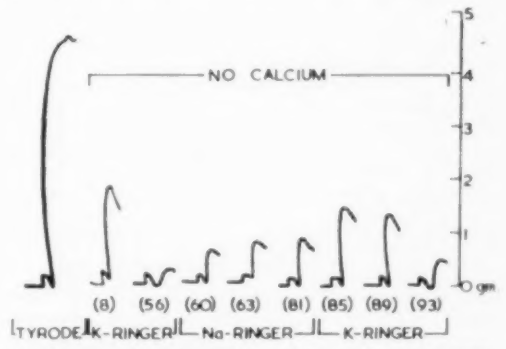

Fig. 3. Effects of acetylcholine (5×10^{-5}, gm./ml.) on rat uterus in calcium-free solutions during successive periods of immersion in sodium chloride–Ringer solution and potassium sulphate–Ringer solution at 23° C. Numbers within brackets denote minutes after removal of calcium chloride from the bath. Note: (1) overall decline of responses due to lack of calcium; (2) increased responses after change from potassium–Ringer to sodium–Ringer solution; (3) initial potentiation of response after change from sodium–Ringer to potassium–Ringer solution

not only are the acetylcholine responses increased when the preparation is changed over to sodium–Ringer, but there also is a further potentiation of the first few acetylcholine responses after re-introduction of potassium Ringer solution. The persistence and slow decay of this effect suggests that immersion in sodium Ringer solution has produced some persistent, slowly decaying alteration in the smooth muscle cell which improves the response to acetylcholine.

To summarize: (1) Calcium ions in low concentrations cause development of tension in the depolarized rat uterus muscle. The tensions produced are submaximal but can be further increased by the application of acetylcholine. (2) Contractions induced by depolarization and by acetylcholine are both dependent on calcium. However, depolarization responses decline more rapidly in the absence of calcium than acetylcholine responses, so that a stage can be reached when acetylcholine is effective but depolarization by isotonic potassium sulphate is ineffective. (3) Acetylcholine causes greater development of tension in polarized than in depolarized smooth muscle preparations. This difference is probably due partly to conducted impulses in the polarized muscle and partly to some other factor, so far unexplained.

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Influence of Changes of Blood Volume on the Concentration of Aldosterone in Peripheral Plasma of Intact Unanæsthetized Dogs

Investigations by F. C. Bartter *et al.* and by G. Farrell and his collaborators[1] on the regulation mechanism of aldosterone secretion have indicated a close relationship between blood volume and the production-rate of the hormone aldosterone. The effect of changes of fluid volume has been studied by these authors, measuring the aldosterone secreted in the urine or in the adrenal venous blood. None of these methods tells anything definite about variations of the concentration of hormone in the peripheral blood. As the action of the hormone in the organism is supposed to be closely dependent on the concentration in peripheral blood, it is of great interest to follow these concentrations directly, and information about the latency of variations may prove to be useful for the elucidation of the nature of regulation of the level of the hormone.

The double-isotope derivative method for determination of cortisol described by Bojesen[2] has been refined to the low level of aldosterone in peripheral plasma[3]. Using this method, we have examined the effect of bleeding, blood transfusion, infusion of a dog Ringer's solution, and infusion of dog Ringer's solution made up with 5 per cent dextran, on the concentration of aldosterone (extractable with chloroform) in the peripheral plasma of dogs. Docile dogs were selected for the experiments, which lasted about 1½ hr., during which the animals were lying on a table. Being accustomed to this, the animals were not agitated during the experiments. They had been fed with a diet low in salt (pork meat, potatoes, distilled water) for more than a week before the experiments were carried out. In all cases, a sample of blood, about 30 ml., was taken from the saphenous vein or the femoral artery just before the treatment to be studied was given. This was finished within 2–5 min. from zero time. Blood samples were then collected at intervals of about 20 min. during 1 hr. In the bleeding experiments, the blood was collected from the femoral artery into a sterilized transfusion bottle, using citrate as an anticoagulant. The blood was given to the same dog through the saphenous vein 3–4 days later, in the transfusion experiment. The dog Ringer's solution employed has been described previously[4] and is a solution imitating an ultrafiltrate of the plasma of normal dogs. The dextran used was 'Dextran 150' (Pharmacia, Copenhagen). As it was found in preliminary experiments that the dog Ringer–dextran solution, when infused, had the same depressing effect on the aldosterone-level as had the blood transfusion, every blood sample was simultaneously compensated for by injection of an amount of Ringer–dextran solution equal to the amount of plasma taken from the animal. Besides the experiments mentioned, in which the fluid volumes taken from or given to the dogs were 200–250 ml., control experiments were carried out, in which no change of the blood volume of the animal was induced, the samples being compensated for by dog Ringer–dextran solution as mentioned.

Table 1. Response of Plasma Aldosterone to Induced Changes in the Blood Volume by Different Means

The figures in parentheses indicate the interval of time between the induced change in blood volume and the collection of the blood sample. With the amount of plasma analysed (15 ml.), 5 ngm. per 100 ml. is the lower limit of sensitivity of the method

Type of experiment	Dog	Aldosterone in plasma ngm. per 100 ml. (time, min.) 1	2	3	4
Bleeding	*C*, ♀, 22 kgm.	33 (0)	162 (22)	156 (39)	236 (72)
	M, ♂, 18 kgm.	7 (0)	29 (14)	31 (30)	23 (62)
	J, ♂, 17 kgm.	31 (0)	41 (16)	51 (38)	59 (64)
Blood transfusion	*C*	40 (0)	26 (15)	14 (30)	10 (50)
	M	40 (0)	16 (22)	23 (42)	13 (67)
	A, ♂, 15 kgm.	51 (0)	14 (30)	10 (43)	8 (60)
Dog Ringer's solution	*M*	45 (0)	19 (20)	11 (50)	17 (65)
	M	46 (0)	44 (25)	16 (50)	25 (65)
	M	28 (0)	18 (22)	12 (45)	17 (65)
Dog Ringer–dextran	*M*	100 (0)	39 (22)	16 (37)	20 (58)
	J	55 (0)	14 (14)	12 (29)	5 (45)
Control	*J*	5 (0)	5 (21)	13 (56)	8 (82)
	J	17 (0)	20 (18)	17 (33)	19 (58)

The results (Table 1) are as might be expected from the previous work by others[1]. The very marked difference between the level of aldosterone in the first and the second blood samples except in the control experiments clearly shows that the blood volume is directly related to the level of aldosterone by means of a very rapid mechanism. As the rates of elimination and production will both influence the level in the peripheral plasma, the results do not lead to a final conclusion concerning the latencies of the regulation of the rate of production. In the case of bleeding, a comparison with the results obtained in

similar experiments with the collection of adrenal venous blood suggest, however, that decreased elimination is not a main factor. In the case of transfusion and infusion experiments with dog Ringer–dextran, the steep slope of the plasma curve indicates that if the rate of elimination were a main factor, the increase of rate required is too great to be likely. Therefore our results suggest that the mechanism by which aldosterone secretion is regulated operates with a latency of a few minutes in relation to changes in the blood volume.

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Œstrogen Antagonisms: 19-Norprogesterone and 18,19-Dinortestosterone as Œstrone Antagonists

CLEAVAGE of the angular methyl group at carbon-10 of the testosterone molecule results in a compound that is much more potent than the parent as an œstrogen antagonist (unpublished work) and myotropic agent[1], but not as an androgen[1]. Since 19-norprogesterone has been known as a potent progestational agent for some years[2] and 18,19-dinortestosterone has recently been synthesized by Dr. W. F. Johns, of the Division of Chemical Research, G. D. Searle and Co., these two materials have been examined as antagonists of œstrone-induced vaginal smear changes in spayed mice.

The assay will be described in detail elsewhere (unpublished work). Spayed, adult, female mice were selected from a colony and injected with a total dose of 2 μgm. of œstrone, given in four equal, daily, subcutaneous injections over a 4-day period. Vaginal smears were taken on the afternoon of day 5 and morning of day 6, and were scored as positive if no leucocytes were present[3]. The standard dose of œstrone produced 80–100 per cent positive responses in various tests with 10–15 mice in a group. Comparisons between and among compounds were made at the dose-level that was estimated to produce a 50 per cent depression in this response.

Table 1. EFFECTS OF PROGESTERONE, 19-NORPROGESTERONE AND 18,19-DINORTESTOSTERONE AS ANTAGONISTS OF THE VAGINAL SMEAR EFFECTS OF 2 μGM. OF ŒSTRONE

Dose: œstrone 2 μgm. + other steroid	Progesterone: No.	Progesterone: No. positive	Progesterone: Per cent positive	19-Norprogesterone: No.	19-Norprogesterone: No. positive	19-Norprogesterone: Per cent positive	18,19-Dinortestosterone: No.	18,19-Dinortestosterone: No. positive	18,19-Dinortestosterone: Per cent positive
0	33	30	91	29	28	97	14	14	100
1				13	12	92			
3				13	11	85			
10	28	21	75	27	13	48			
30	35	30	86	26	8	31	14	12	86
100	36	19	53	14	1	7	14	14	100
300	25	12	47	14	0	0	15	15	100
1,000	17	0	0				14	14	100

Approximate ED_{50}: progesterone, 180 μgm.; 19-norprogesterone, 14 μgm.; 18,19-dinortestosterone, >1,000 μgm.

19-Norprogesterone is some thirteen times more potent than progesterone as an antagonist of the vaginal smear effects of œstrone (Table 1). 18,19-Dinortestosterone had no effect on the proportion of positive responses at doses up to 1,000 μgm. (This dose of 18,19-dinortestosterone produced slight but significant inhibition of the uterine growth stimulated in immature mice by 0·3 μgm. of œstrone.)

The high potency of 19-norprogesterone correlated well with previous results in which the 19-nor-configuration was more potent than the natural form (unpublished work). The absence of activity of 18,19-dinortestosterone is of particular interest; cleavage of the angular methyl group at carbon 10 increases the potency of testosterone (80–170 per cent, unpublished work) as an œstrone antagonist, whereas with the further cleavage of the methyl group at carbon 13 activity is largely lost.

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RADIOBIOLOGY

Lead-210 in Some Human and Animal Tissues

IN two recent publications[1,2] measurements have been reported of the levels of lead-210 (radium-*D*) in the bones of non-occupationally exposed American subjects. In the present communication similar findings are reported for some human and animal bone and liver specimens from Great Britain.

Six samples of bone, obtained from subjects who had died of malignant disease, were analysed for both total lead and lead-210. The specimens were dry ashed at 470–500° C., using lead-free concentrated nitric acid as an ashing aid. After solution of the ash in lead-free hydrochloric acid, lead was extracted with diethyl-ammonium diethyl-dithiocarbamate at *p*H 0·1 and then estimated colorimetrically using dithizone, lead-210 being estimated afterwards by low-background beta counting of the daughter bismuth-210, which was separated from lead with cupferron (to be published). The results are given in Table 1. It will be seen that the mean stable lead concentration was 6·3 μgm./gm. bone, in good agreement with the value of 6·6 μgm./gm. found by

Table 1

Tissue	Stable lead (μgm./gm. wet bone)	Lead-210 (picocurie/gm. wet bone)
Human vertebra	6·8	0·026
Human vertebra	4·4	0·029
Human vertebra	8·9	0·025
Human vertebra	8·7	0·034
Human vertebra	4·0	0·022
Human tibia	4·5	0·021
Mean	6·3	0·026
Ox bone (shaft)	3·8	0·26
Ox bone (shaft)	2·4	0·24
Mean	3·1	0·25

Tipton[3]. The mean lead-210 concentration of 0·026 picocurie/gm. of bone is comparable with the values found by Hursh[1] at Rochester, and Holtzman[2] at Argonne, of 0·015 and 0·040 picocurie/gm. respectively.

At the same time, measurements have been carried out to determine the nature of the α-radioactivity previously reported[4] in the liver of seven non-occupationally exposed individuals at levels of the order of 0·34 picocurie/gm. ash, equivalent to about 0·003 picocurie/gm. tissue. Using an improved version of our sensitive α-spectrometer (ref. 5, and to be published), α-spectra have been obtained of the ashed liver of two other unexposed individuals (both malignant cases, as were also the earlier subjects). These show at least 80 per cent of the activity in a single spectral line at approximately 5·3 MeV., corresponding to polonium-210. One of these spectra is shown in Fig. 1. Since it is to be expected that most of the polonium present in the original sample would be volatilized during ashing, the subsequent observation of polonium-210 in the ash is presumably indicative of the presence of its parent lead-210. Although these identifications have so far been made for two individuals only, it seems reasonable to suppose that some 80 per cent or more of the total α-activity previously reported for the larger group of liver samples (that is, approximately 0·0025 picocurie/gm. of wet tissue) was also due to the presence of lead-210.

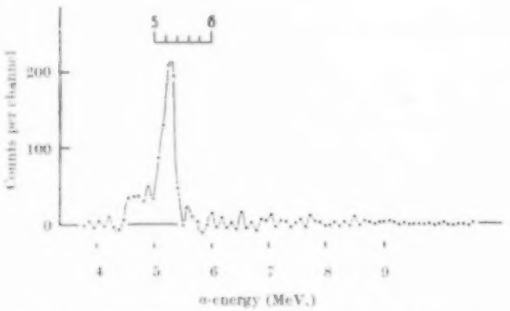

Fig. 1. α-Particle spectrum of a sample of human liver ash

We have also measured the total lead and lead-210 contents of two samples of ox bone. The results, included in Table 1, indicate that the lead-210 contents are some ten times higher than for humans, although the total lead contents of ox bone are lower by a factor of two. By means of α-spectroscopy, supported by observations of the rate of growth of total α-activity after ashing, the lead-210 content of a sample of ox liver was found to be approximately 0·05 picocurie/gm. of tissue, some twenty times greater than the value reported above for human beings. It appears that the relatively high levels of lead-210 in the ox may be attributable to the previously reported occurrence of this nuclide on foliage[6].

We wish to acknowledge the support and encouragement of Prof. W. V. Mayneord in this work, and our thanks are also due to Dr. W. Anderson and Mr. J. O. Crookall for helpful discussion. We are indebted to Dr. J. P. M. Bensted of this Department, and to Dr. N. F. C. Gowing, director of the Department of Pathology, Royal Marsden Hospital, for providing post-mortem material. Financial support for one of us (Z. S. J.) was provided by the International Atomic Energy Agency.

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Incorporation of Phosphorus-32 into Adenosine Triphosphate of Adrenal Chromaffin Granules

The discovery by Hillarp and his colleagues[1] of the presence of large amounts of adenosine triphosphate (ATP) in the adrenal medulla has led to speculations on its role in the storage and retention of catechol amines in this tissue. It has been shown that the amines are stored in cell organelles, the chromaffin granules, which are distinct from the mitochondria; they can be separated from the latter by centrifugation over a density gradient[2]. This has made it possible to establish that ATP occurs in a high concentration in the sites of storage of the catechol amines, in stoichiometric amounts in relation to the amines present.

It is known from work on many different types of cells that the mitochondrial ATP is rapidly turned over; but it is not known if the same holds for the ATP in the chromaffin granules. Either the main function of the ATP is to act here as the anion that holds the catechol bases in the storage position, or it serves as an energy donor in maintaining the high concentration of amine in this site against a diffusion gradient. Thus, some insight into the function of the ATP might be gained by a study of the incorporation of phosphorus-32 into the ATP of chromaffin granules, as compared to that in the mitochondria.

Animals received 0·5–1·0 mc. ^{32}P/kgm. body-weight 0·5–2 hr. before death. The rats were killed by decapitation and the adrenals were rapidly removed, adherent fat was dissected away and the glands were dropped into 0·3 *M* sucrose at 0°. The dog was anæsthetized with pentobarbitone before death and the cats were killed by cervical fracture. The mitochondria and chromaffin granules were separated by density-gradient centrifugation and deproteinized with trichloroacetic acid, which was then removed with ether. ATP in the granules was measured by the firefly method[3] and its phosphorus-32 activity was obtained after chemical hydrolysis. Good agreement was found between chemical and firefly estimations, a result which suggests that the predominant nucleotide was ATP. ATP in the mitochondria either was determined chemically as inorganic phosphate liberated by 15 min. hydrolysis in *N* hydrochloric acid at 100°, or the nucleotides were separated on 'Dowex' columns[4], the phosphorus-32 was counted and the concentration determined by the firefly method.

Table 1. Incorporation of Phosphorus-32 into Adrenal Mitochondria and Chromaffin Granules

Species	Time after injection (hr.)	Specific activity*	
		Mitochondria	Granules
Cat	0·5	285	< 5
	2·0	465	—
Rat	1·0	65	< 5
	1·0	78	< 5
	1·0	66	13·5

* Specific activity as counts/min./μgm. phosphorus.

It will be observed (Table 1) that in both the cat and the rat the specific activity of granular ATP was very much less than that of the mitochondrial ATP. With these two species the adrenal cortex was not separated from the medulla so that the mitochondrial fraction represented material from two different parts of the gland. Since these could have different turnovers of ATP, an experiment was performed with a dog, with which species separation of the two regions of the gland could be achieved before isolation of the mitochondria. Although Spiro and Ball[5] have reported that the respiratory enzymes in the cortex of bovine adrenals are several times more active than those in the medulla, at 1 hr. after administration of phosphorus-32 to the dog, the specific activity of the ATP (separated on 'Dowex') of the cortex was only 50 per cent greater than that of the medullary mitochondria. Therefore, it seemed unlikely that the large differences in specific activity of ATP between cat and rat mitochondria and granules was due to ATP of high specific activity from the cortical mitochondria exaggerating a very low activity from the medullary mitochondria.

The presence of ATP in different cell compartments with different turnovers has been discussed by Chance[6], with reference to mitochondria and cytoplasm, and a distinction between nuclear and cytoplasmic ATP metabolism has also been observed (Ord, M. G., and Stocken, L. A., unpublished work). The low uptake of phosphorus-32 in the granule fraction could be readily understood if we assume that the ATP is functioning in the granules as a relatively inert binding anion for the catechol amines, rather than as an energy donor concerned with maintenance of their concentration. It is hoped to obtain further evidence on this point by a study of the uptake of phosphorus-32 into ATP during the restoration of catechol amines after depletion of the granules.

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PATHOLOGY

Production of Pyrogenic Substances by Extracts of Delayed Hypersensitive Cells mixed with Antigen *in vitro*

Many published experiments on the passive transfer by cells of hypersensitivity undoubtedly indicate that the mechanism of delayed (tuberculin) hypersensitivity is based on a reaction of hypersensitive cells with antigen. In previous work I have demonstrated that, on incubation of delayed hypersensitive cells with antigen *in vitro*, substances are formed imitating manifestations of delayed hypersensitivity, namely, fever and inflammation of the skin[1]. Simultaneously with the formation of pyrogenic substances, the cells are desensitized, that is, they lose the ability to transfer passive hypersensitivity[2].

The question whether a similar reaction (formation of pyrogenic substances) could be evoked when mixing and incubating cell-free extracts of hypersensitive cells with specific antigen has now been investigated.

Sensitization of the animals (guinea pigs, rabbits), preparation of cell suspensions from spleen and lymph nodes, antigen used (2 μgm. purified protein derivate or 0·5 L_f purified diphtheria toxoid), and the method of evaluation of the fever reactions have been described in detail elsewhere[1]. A positive reaction is manifested by a short monophasic fever beginning usually within 15 min. and culminating in 30 min. after injection of the substance tested to normal, non-hypersensitive animals.

Cell-free extracts were prepared either by repeated (8–10 times) freezing and thawing or by ultrasonic radiation; active substances are released even on 24-hr. storage of hypersensitive cells in Hanks's solution at + 4° C. In the preparation of the extracts the decrease of the cell count was followed, and also the loss of staining characters as viable cells, as well as the increase of protein substances in the supernatant fluid.

A typical experiment is reported in Table 1. Neither the cell-free extract of hypersensitive cells nor the antigen is found to be pyrogenic. The mixture of these substances is pyrogenic, irrespective of the incubation period; pyrogenicity is developed even when the antigen and the cell-free extract are mixed and injected immediately to the test animals. It is evident from Table 1 that not even a 10-fold quantity of antigen or 5-fold amount of cell-free extract is capable of evoking pyrogenic reaction by itself. The same results were obtained in a number of experiments with rabbits and when mixing extracts

Table 1. Pyrogenic Activity of Cell Extracts of Guinea Pigs sensitized by B.C.G. Vaccine mixed with Tuberculin *in vitro*

Substance tested	*In vitro* incubation period	Temperature changes in recipients (deg. C.)
Cell extract, 1 ml.	—	0 0·2 0·2
" " 5 ml.	—	−0·1 0·2 0·1
Purified protein derivate 1γ	—	0 0 0·1
10γ	—	0 0·1 0·2
Cell extract, 1 ml. + 1γ purified protein derivate	20 hr.	0·6 0·8 1·1
" " "	2 hr.	0·8 1 1·3
" " "	30 min.	0·7 0·9 1·1 1·4
" " "	none	0·8 0·9 1·2 1·3
Diphtheria toxoid, 0·5 L_f	—	0 0·1 0
Cell extract + diphtheria toxoid, 0·5 L_f	various	0 0 0 0·1 0·1 −0·2 −0·2 0

of diphtheria toxoid hypersensitive cells with the specific antigen. Extracts of normal cells mixed with antigen or extracts of hypersensitive cells mixed with the non-specific antigen yield completely negative results.

The effective substance (factor giving rise to pyrogenicity on mixing with antigen) can be stored in the frozen state. Its physical and biochemical properties and further biological effects are under investigation.

A few observations can be found in the literature concerning the possibility of passive transfer of delayed hypersensitivity by cell-free extracts in laboratory animals[3] and especially in man (so-called 'transfer factor')[4]. The appearance of pyrogenicity (as a manifestation of delayed systemic hypersensitivity)[5] in the reaction of hypersensitive cell extracts with antigen *in vitro* is in agreement with the experiments reported.

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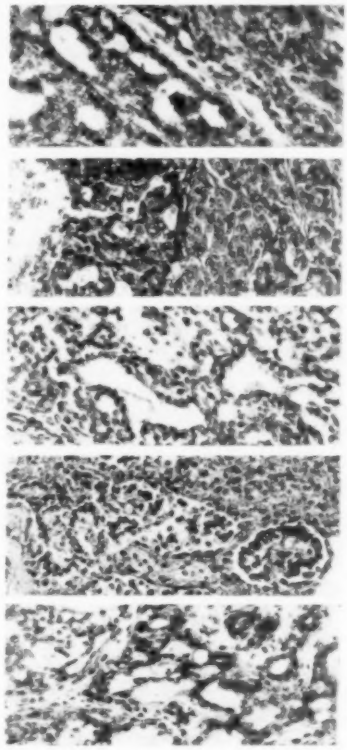
Induction of Mammary Carcinoma in Hypophysectomized Rats treated with 3-Methylcholanthrene, Œstradiol-17β, Progesterone and Growth Hormone

The rapid induction of mammary carcinomas in rats treated by intra-gastric administration of 3-methylcholanthrene has been described by Huggins, Briziarelli and Sutton[1]. It was afterwards shown by Huggins, Grand and Brillantes[2] that the physiological state of the mammary tree was critical in the development of such tumours, and they were unable to induce mammary carcinomas in hypophysectomized rats. The present report describes the induction of mammary carcinomas in hypophysectomized rats which were treated intra-gastrically with 3-methylcholanthrene and in which partial replacement therapy was attempted with œstradiol-17β, progesterone, and growth hormone.



Figs. 1–5. Photomicrographs of tumours from rats 1–5 respectively. (Hæmotoxylin and eosin. × 135)

The pituitaries of female Sprague–Dawley rats were removed when they were 50 days old, when they weighed between 150 and 170 gm. Treatment was begun 13 days after hypophysectomy according to the following scheme.

(1) Œstradiol-17β, 1 μgm. and progesterone, 4 mgm. in 0·2 ml. sesame oil subcutaneously daily for 6 days every week.

(2) 3-Methylcholanthrene, 10 mgm. dissolved in 1 ml. sesame oil, intra-gastrically, once weekly.

Table 1

		Rat 1	Rat 2	Rat 3	Rat 4	Rat 5	Rat 6
Age at hypophysectomy	(days)	50	50	50	50	50	50
Age at first injection	(days)	64	64	64	64	64	64
Weight at operation	(gm.)	150	172	150	166	158	166
Weight at death	(gm.)	354	353	320	296	363	251
Weights of organs at death:							
Heart	(mgm.)	935·5	1,070	867	1,274	1,350	1,615
Kidneys (right and left)	(mgm.)	2,105	2,515	2,140	1,855	2,872	2,008
Spleen	(mgm.)	427·5	625	378	565	640	824
Adrenals (right and left)	(mgm.)	28	23	28	22	34	28
Ovaries (right and left)	(mgm.)	16	43	42	110	165	82
Uterus	(mgm.)	462	509	534	620	632	654
Total dose of œstradiol	(μgm.)	121	142	160	164	189	214
Total dose of progesterone	(mgm.)	484	568	640	644	669	694
Total dose of methylcholanthrene	(mgm.)	210	240	270	280	320	360
Total dose of growth hormone	(mgm.)	161	224	282	298	398	498
Duration of treatment	(days)	141	165	186	191	220	249
Incubation period	(days)	102	147	122	170	184	220
Site of tumours		5 R., 3 L.	1 R.	2 L., 3 L.	2 L.	3 R., 4 L.	4 L.
Size of tumours at death	(mm.)	15 × 15 × 10 10 × 10 × 5	15 × 15 × 10	6 × 6 × 4 3 × 3 × 2	15 × 15 × 3	15 × 15 × 15 40 × 40 × 30	10 × 7 × 3
Nature of tumours		Adeno-carcinoma	Adeno-carcinoma	Adeno-carcinoma	Necrotic adeno-carcinoma	Adenocarcinoma Sarcoma	Sub-epidermal basal cell tumour of skin

(3) Bovine growth hormone, 0·5 mgm. in 1 ml. saline daily for 6 days every week, rising to 1 mgm. then 2, then 3 and finally 4 mgm./rat/day after intervals of 48, 31, 35 and 36 days respectively.

Mammary gland tumours developed in five rats out of nine. Histologically each tumour had the structure of an adenocarcinoma with some areas of comparative anaplasia. Nuclei were small, and regular in size and shape. One tumour, in rat No. 4, was almost entirely necrotic. In addition to its mammary gland tumour, rat No. 5 developed a spindle-celled sarcoma which grew rapidly; and rat No. 6 developed a sub-epidermal basal cell tumour of skin but no mammary tumour. Relevant data concerning these rats are given in Table 1 and illustrations of the mammary tumours in Figs. 1–5.

It is evident that partial replacement therapy with oestradiol, progesterone and growth hormone, as in the present experiments, permits hypophysectomized rats to develop mammary carcinomas following the administration of methylcholanthrene. This is in keeping with experiments of Nandi and Bern[3] who found that the development of hyperplastic mammary nodules to carcinomas in mice, required the presence of steroids together with either growth hormone or prolactin from the pituitary; and of Kim and Furth[4] who found that growth of mammary carcinomas in rats, stopped by hypophysectomy, could be restarted by the implantation of pituitary tumours known to secrete mammotrophin.

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HÆMATOLOGY

Identity of the α-Chains of the Minor Human Hæmoglobin Components A_2 and A_2' with the α-Chains of Human Hæmoglobin *A* and *F*

THE occurrence of a minor hæmoglobin component (A_2' or B_2), which is related to the well-known hæmoglobin fraction A_2, has recently been described[1,2]. This variant, found in families of a Negro community of James Island, is characterized by a very low mobility at an alkaline *p*H. The electrophoretic pattern (at *p*H 8·8) of the hæmoglobin of a person heterozygous for this abnormality, shows a major hæmoglobin fraction (A_0), the fast moving fraction (A_1), the slow moving hæmoglobin A_2, and the hæmoglobin A_2' with a still lower mobility. The hæmoglobin A_2 and hæmoglobin-A_2' are present in equal amounts (0·8–1·2 per cent), the sum of both being equal to the percentage of hæmoglobin A_2 present in the blood of a normal individual. The hæmoglobin A_2' has also been demonstrated in cases with sickle cell trait[2], indicating that the two abnormalities ('double A_2 spot' and 'the presence of the abnormal hæmoglobin *S*') are controlled by a different pair of alleles. In some cases of thalassæmia trait both hæmoglobin A_2 fractions were found to be increased by a factor of two[1,2], the 'double A_2 spot' being contributed by one parent and the thalassæmia trait by the other parent.

The abnormal hæmoglobin A_2' is not rare in the Negro population of the State of Georgia. In the course of a search for hæmoglobin abnormalities of some 300 cases, using the starch gel electrophoretic technique[3,4], the double A_2 spot abnormality was found in members of at least eight families. In all cases the relative amounts of hæmoglobin A_2 as well as of hæmoglobin A_2' were about 1 per cent each (estimated with CMC chromatography[5]). In two cord blood hæmoglobin samples minor amounts (0·2–0·5 per cent) of these two fractions were demonstrable. The occurrence of hæmoglobin A_2' in cases with known hæmoglobin abnormalities (including thalassæmia) has not yet been recorded in our investigations.

Since a close relationship between the hæmoglobin A_2 and the hæmoglobin A_2' seems likely, a study of possible identical structural abnormalities was undertaken. In this communication we report part of the results of this work, namely, some hybridization experiments carried out in order to demonstrate the possible identity of the β-chains of the two minor hæmoglobin components with the α-chains of normal hæmoglobin *A* and hæmoglobin *F*. Large quantities of hæmoglobin A_2 and hæmoglobin A_2' were prepared by CMC-chromatography[5,6] using a 30 cm. × 3 cm. column and 0·01 *M* phosphate buffers of *p*H values ranging from 7·3 to 7·9 as eluting solvents. The dilute hæmoglobin solutions obtained after elution were concentrated on a small CMC column[6] and finally dialysed against distilled water. Small amounts of these components (10–20 mgm.) were mixed with equal amounts of Bart's hæmoglobin, prepared from the blood of cases described before[7]. The mixtures were dialysed at 4° C. against 0·1 *M* sodium acetate buffer (*p*H 5·9) for 36 hr. followed by dialysis for 36 hr. with a 0·01 *M* phosphate buffer of *p*H 6·8. Chromatographic separations of these mixtures before and after hybridization were carried out as described before[4–6]. The results obtained are presented in Fig. 1. In both control experiments (Bart's hæmoglobin + hæmoglobin A_2 and Bart's hæmoglobin + hæmoglobin A_2') the two major fractions are present while minute amounts of hæmoglobin *A* (and also of hæmoglobin A_2 in the mixture of Bart's hæmoglobin + hæmoglobin A_2') as impurities were demonstrable. After hybridization, however, considerable amounts of a hæmoglobin fraction were found, which showed the same mobility in CMC-chromatography as hæmoglobin *F*. The fœtal character of this component was proved by its high resistance towards alkali[8] and by its ultra-violet spectral absorption. It seems, therefore, that fœtal hæmoglobin is formed when hæmoglobin A_2 as well as hæmoglobin A_2' is hybridized with Bart's hæmoglobin. Since both hæmoglobin A_2 and hæmoglobin A_2' are composed of two different polypeptide chains (α- and δ-chains) with chromatographic properties (as tested on 'Amberlite *IRC*' 50 (ref. 4) similar to the α- and the β-chains of normal human hæmoglobin *A*,

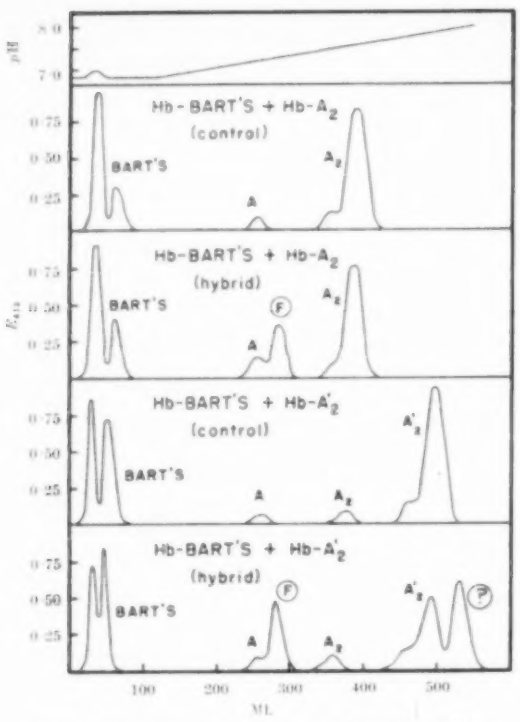

Fig. 1. Chromatographic separation on carboxymethyl-cellulose of mixtures of haemoglobin A_2 (Hb-A_2) or haemoglobin A_2' (Hb-A_2') and of Bart's haemoglobin before and after hybrid formation

and since Bart's haemoglobin consists solely of the γ-chains of haemoglobin-F the following equations seem probable:

$$\alpha_2^A\delta_2 + \gamma_4^F = \alpha_2^A\delta_2 + \gamma_4^F + \alpha_2^A\gamma_2^F + \delta_4 \quad (1)$$

$$\alpha_2^A\delta_2' + \gamma_4^F = \alpha_2^A\delta_2' + \gamma_4^F + \alpha_2^A\gamma_2^F + \delta_4' \quad (2)$$

It thus seems probable that the α-chains of haemoglobin A_2 and haemoglobin A_2' are identical with the α-chain found in haemoglobin F and haemoglobin A since the α-chains of haemoglobin A_2 and haemoglobin A_2' produced foetal haemoglobin after transfer of chain components with Bart's haemoglobin by the hybridization technique. The components δ_4 and δ_4' formed during hybrid formation were not definitely recorded in our chromatographic experiments. It may be that both fractions possess chromatographic mobilities similar to that of haemoglobin H (β_4^A), which is indistinguishable from Bart's haemoglobin under our experimental conditions. It is also possible that the δ_4 component is eluted at the same pH as is haemoglobin A_2 and the δ_4' component at an elution pH value slightly higher than found for haemoglobin A_2' (Fig. 1). Further work, however, was not possible because of lack of material.

Our results support the hypothesis that possible structural differences between both minor haemoglobin components and haemoglobin A and between the two minor haemoglobin fractions itself must lie in the δ-chains of the proteins.

Full extension of our results of differences between these two components and normal human haemoglobin A will be given elsewhere. This work was supported in part by Public Health Service Research Grant No. H-5168 from the National Heart Institute, Public Health Service.

Note added in proof. Since this article was submitted, we have found a homozygous Hb-A_2' or (Hb-B_2) carrier with 2·1 per cent Hb-A_2' and no Hb-A_2.

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CYTOLOGY

Aggregation of Protein Particles in Tumour Cells

In the cytoplasm of the cells of some tumours (Ehrlich ascites tumour, Yoshida ascites tumour, Walker carcinoma, hepatoma of the rat and human malignant lymphogranuloma) a form of dispersion of the ribosomes has been seen[1–3] at the electron microscope described[4–6] as 'scattered' or 'unorganized ergastoplasm'. A similar condition also occurs[8,7] during the previtellogenesis of the oocytes in some animal species (*Haliotis lamellosa*, *Paracentrotus lividus*, *Sphaerechinus granularis*, *Arbacia lixula*). While in tumour cells 'scattered ergastoplasm' persists, it is seen[8] that in the oocytes the ribosomes, after having increased and probably having undergone a transformation, aggregate during vitellogenesis to make yolk globules (Figs. 1 and 4).

It was supposed therefore that in tumour cells there might also occasionally be found formations deriving from the aggregation of protein particles. I have now shown this to be the case.

Fragments of Walker tumour of the Wistar albino rat were put for 5 hr. at room temperature (about 22° C.) in an aqueous solution of deoxyribonuclease ('Crystalline' of Light and Co., 10 mgm./ml., non-activated). At the same time controls were kept on fragments not treated with enzyme, and on fragments kept for the same time at room temperature in distilled water only. In each case the fragments were fixed in a 1 per cent solution of osmic acid (buffered by Palade's method). For observation under the optical microscope, the fragments were embedded in paraffin; for observation in the electron microscope they were placed in a mixture of butyl and methyl methacrylate.

Preparations and observations were made at the Centre for Electron Microscopy at the University of Padua with a Siemens Elmiskop I*a* apparatus. Under the optical microscope cells notably swollen through absorption of water were observed in the preparations treated with enzyme; in the cytoplasm of those cells of the outer layers of the sections some very evident globules of various sizes (Figs. 2, 3) of a similar character to those of the yolk of some oocytes (Fig. 1) appeared. These globules have not hitherto been found either in control preparations or, at least

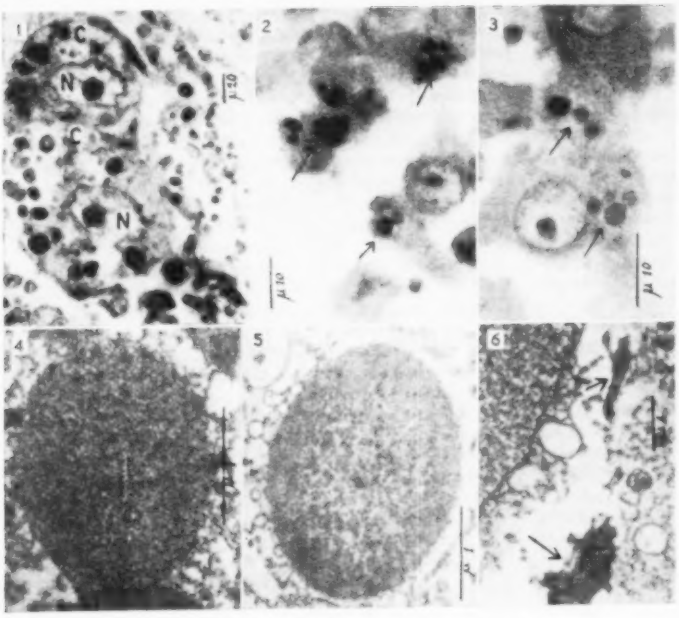

Fig. 1. Two oocytes of *Aplysia depilans*; *C*, cytoplasm with yolk globules; *N*, nuclei with nucleoli. Figs. 2 and 3. Walker tumour cells with globular formations (arrows) in a preparation treated with deoxyribonuclease. Fig. 4. Yolk globule of oocyte of *Paracentrotus lividus* derived from aggregation of granulations. Fig. 5. Globular formation of Walker tumour cell, treated with deoxyribonuclease, derived, like the yolk globule of Fig. 4, from an aggregation of granulations. Fig. 6. Portion of a Walker tumour cell kept for control in distilled water. Note the accumulations of granulations with completely irregular aspects (arrows). Figs. 1, 2 and 3, under the optical microscope; Figs. 4, 5 and 6, in the electron microscope

so far as can be seen with the optical microscope, in the cells of the more internal parts of the sections of the preparations treated with enzyme.

In the electron microscope some globular formations (Fig. 5) manifestly derived, as in the oocytes (Fig. 4), from an aggregation of granulations (ribosomes) were always seen in the cytoplasm of the cells of the tumour undergoing enzyme action. These formations, corresponding evidently to the globules seen under the optical microscope, are very variable in number and size in each cell. In the cells of the control preparation, kept in distilled water, other accumulations of granulations, but with completely irregular aspects occurred (Fig. 6).

These results must be supported by other experiments, made also in a proper isotonic and isohydrogenionic medium. It has to be established if the deoxyribonuclease, too, constitutes the only substance which can determine the process of aggregation, or rather what, like other substances, is suitable for creating the favourable conditions for this process to take place. The same result, in any event, appears to be of notable importance in connexion with: (*a*) the existence of an enormous number of unorganized ribosomes; (*b*) the possibility of obtaining their aggregation artificially as normally in the oocytes; (*c*) a new orientation for the understanding of very intense intracytoplasmatic proteic syntheses; (*d*) ascertaining of the real alteration of the tumour cells. The hypothesis[3,7] that the cellular structure, which reacts directly to the action of carcinogenic agents is the nucleolus, would seem to be more and more consistent. In fact, this, by producing the ribonucleoproteic granulations (karyoribosomes) in large quantities, would seem to provoke the transformation of the normal cell into a tumour cell. The principle would lie in a modification of the ribonucleoproteins which, through the presence of the so-called infective ribonucleic acid[9,10], would be induced to self-duplication without control.

All the alterations which, among others, include modifications in the chromosomes, hypertrophy of the Golgi bodies, and noticeable variations in the number of mitochondria[6], would derive from the incapacity of the cell to organize the ribonucleic granulations (cytoribosomes), which flow from the nucleus into the cytoplasm in enormous quantities. The uncontrolled cellular division of tumours would be but a consequence of the uncontrolled divisions of the ribosomes in the nucleus.

Finally, it should be pointed out that the result of artificial aggregation (above), from the theoretical side, is still valuable even if its realization is very rare and difficult. In this connexion the rarity with which very numerous embryos have been found in malignant tumours of the testes[11] and the ovary[12] should be emphasized; these embryos deriving probably from a kind of vitellogenesis (through aggregation of proteic particles as in the normal oocytes) within the germinative cells[7].

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Distribution of Deoxyribonucleic Acid in the Cell Nucleus

The problem discussed in this communication is the state of intermitotic chromosomes, and since deoxyribonucleic acid (DNA) is characteristic of the chromosomes it is the distribution and localization of the structure carrying DNA in the nucleus which are to be examined.

This question of distribution of DNA is of importance for the cytophotometric method of Pollister and Ris[1] measuring the relative DNA content of a Feulgen-stained nucleus. This method assumes a more or less regular distribution of DNA in the nucleus. Indeed, different investigations concerning the state of the intermitotic chromosomes have shown that they are in a very extended and hydrated state and differ in this way from the condensed and dehydrated mitotic chromosomes. According to a model first designed by Pollister[2] the swollen chromosomes nearly fill the entire nucleus. Investigations of the effects of different dehydrating agents on the nuclear structure, as we see them in the phase-contrast microscope, have confirmed this idea[3].

Recently, another interpretation of the distribution of DNA was proposed: according to Iverson's observations[4], the DNA-carrying structure is distributed in a peripheral zone of the nucleus and the remaining observed Feulgen-stained masses would be the 'nucleolus associated chromatin'. According to Iverson's illustrations, the remaining interior of the nucleus is empty and free from DNA. Similar findings have been reported by Ludford[5].

My investigations with paraffin sections fixed in various ways (non-buffered formol, Carnoy's, Stieve's, Zenker's solution, Susa mixture) have not confirmed Iverson's findings unless the preparations were dehydrated very rapidly in alcohol or were fixed in absolute methyl alcohol or formalin at *p*H 4·0. In normal dehydrated preparations the Feulgen-stained masses were not only on the peripheral membrane or adjacent to the nucleoli but also distributed throughout the remaining nuclear compartment. It is known that most fixing agents precipitate the proteins, especially the nucleoproteins, the intensity of the precipitation being subordinated to the *p*H, the destruction of the lipoids and many other factors[6]. This relationship of dehydration and the milieu can be followed with the phase-contrast microscope[7].

Fig. 1. Feulgen squash method, phase contrast. Nucleus from the epithelium of the colon of a female rat photographed at three different levels. Small and large chromatin granules can be seen in the nucleus

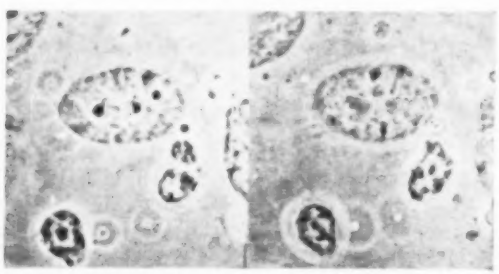

Fig. 2. Carmine acetic acid squash method, phase contrast. Nucleus from the epithelium of the small intestine of a female rat photographed at two different levels. The whole nuclear compartment is interspersed with granules. Five chromocentres are demonstrated

Squash methods, for example those described by Darlington and La Cour[7], have advantages over the paraffin section method for demonstration of the nuclear structure. With these squash methods the nuclei to be observed should not be flattened, that is, they should move freely with the current existing in the fluid between slide and cover-slip. By moving the fine adjustment one can convince oneself that, using the Feulgen-staining method[8] or the carmine acetic acid stain[9], the DNA-containing material is more or less equally distributed throughout the whole nucleus (Figs. 1 and 2). Although much chromatin accumulates directly on the inner face of the nuclear membrane, it is also often distributed without any evident order in the interior of the nucleus especially when the nucleolus also is situated in the interior. Extended research on the nuclei of different tissues has demonstrated that the distribution of the DNA-containing chromatin in the nucleus is specific with every tissue and that this specificity is lost in cancerous cells as a result of dedifferentiation[10].

These observations illustrate the fact that the DNA-carrying chromosomes are interspersed rather evenly in the nuclear compartment.

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Differences in Mechanism of Staining Reaction for Mast Cells of Some Lower Vertebrates

I have examined the differences in staining reactions in the mesenterial and myocardial mast cells of the viviparous Cyprinodonts *Lebistes reticulatus*, *Xiphophorus helleri* and *Xiphophorus maculatus*[1], the mesenterial mast cells of the carp *Cyprinus carpio* and in the cutaneous mast cells in precancerous skin (carcinoma planocellulare) of the lizard *Lacerta agilis*[1]. Just as in the mast cells of the mouse during the course of experiments on mucopolysaccharide reactivity after peracetic acid oxidation (Greenspan's mixture, 25° C., half an hour)[2], a change was observed in the cytoplasm of the mast cells. When the peracetic acid oxidation was followed by digestion with mucopolysaccharide-hydrolysing enzymes, various staining reactions were obtained by the methods used for mucopolysaccharides.

To permit a satisfactory comparison with the results obtained by Fullmer[3] with the mast cells in the skin, the tongue and other organs of adult *BALB/c* strain mice, I used the corresponding histological technique. Immediately after death by decapitation, excised pieces 2 mm. thick were put into aqueous neutral calcium acetate formalin at 17° C. for a period of 24 hr. (Lillie[3]). After washing

and dehydration, these pieces were embedded in paraffin and sectioned at a thickness of 6μ.

The mast cells were stained in the control sections with aldehyde fuchsin, the Hale stain, the Rinehart stain and azure *A* (0·5 per cent azure *A* in aqueous 0·2 *M* phosphate buffer *p*H 4, at 25° C., half an hour). These mast cells reacted excellently, either with or without previous oxidation of tissue sections with peracetic acid. In general, the peracetic acid appeared to intensify the subsequent staining reactions. Just as in the mouse[3], if the sections were oxidized with peracetic acid and then digested with lysozyme (5 mgm. of lysozyme, Worthington ; 30 ml. of 0·2 *M* phosphate buffer, *p*H 5·3 ; 37° C. ; 24–48 hr.) or with β-glucuronidase (15 mgm. of β-glucuronidase, Nutritional Biochemicals Corp. ; 50 ml. 0·1 *M* acetate buffer, *p*H 4·5 ; 37° C. ; 24–48 hr.) only a few mast cells were affected by aldehyde fuchsin, whereas none was affected by the Hale stain. The few mast cells which reacted with the aldehyde fuchsin were only slightly stained. With azure *A*, however, the granules and the cytoplasm of the mast cells remained strongly reactive. The staining reaction appeared to be only slightly, if at all, reduced. In some cases testicular hyaluronidase (25 mgm. of testicular hyaluronidase, Nutritional Biochemicals Corp. ; 50 ml. 0·2 *M* phosphate buffer, *p*H 6 ; 37° C. ; 24–48 hr.) prevented the subsequent Hale staining reaction. If the sections were not oxidized with peracetic acid (Greenspan's mixture, 25° C., half an hour)[2] prior to the digestion step, no effect on any staining reaction was observed. By boiling for half an hour in alkaline buffer at *p*H 9, the lysozyme was inactivated, which confirms previous work by Fullmer[3]. The mast cells were found to react strongly with all stains after incubation in the usual manner with lysozyme treated in this way.

My results, like those of Fullmer[3], using mast cells of the mouse, are fully compatible with the view that after the peracetic acid oxidation both the lysozyme and the glucuronidase enzymatically remove from the mast cells a certain component which is stainable with the Hale stain and the aldehyde fuchsin, and there remains a component inducing a strong metachromasia with azure *A*. Since the inhibitors, which are not otherwise likely to alter the enzyme, prevent the effect on the staining reactions, Fullmer[3], and rightly in my opinion, maintains that the insufficient staining with the Hale stain and the aldehyde fuchsin in this case represents an uptake of basic protein by acid mucopolysaccharides, rendering these groups inaccessible to the stains. Several authors have described this type of blockage. On the basis of the reactions mentioned above, one can conclude that although, in all the three histochemical methods used, mucopolysaccharides are stained, the staining reactions of granules and other cytoplasmic components of mast cells are not equivalent at all, and probably do not form the same substance with the stain. These results are in agreement with those of Gomori[4], who had noted differences in the degree of staining of various mucopolysaccharides using various methods, and also with the fact that the periodic acid oxidation of tissue sections has been found to induce the staining of certain normally unreactive substances with aldehyde fuchsin, and to alter the susceptibility of oxytaban fibres to lysozyme, hyaluronidase and elastase.

Furthermore, I used for the staining of the mast cells of the lower vertebrates mentioned two new techniques, namely, the night-blue method[5] and tartrazine counter-staining according to the periodic acid – Schiff procedure[6].

The night-blue method is essentially the same as that reported by Hallberg[7], although for the staining of human and mammalian mastocytes by Winkelmann[5] some minor modifications were made. The mast cells of the lizard and the teleost species mentioned above showed a positive orthochromatic night-blue stain in the granules. The nuclei of mast cells were found not to stain, nor did the cytoplasm. After alcohol fixation the stain disappeared completely.

After applying tartrazine counterstaining, following the periodic acid – Schiff procedure, the granules of the mast cells of the lizard, the carp and the viviparous toothcarps stained in a different way from the other granules giving a positive periodic acid – Schiff reaction. As tartrazine, an azo derivative of 1-phenyl-5-pyrazolone-3-carboxylic acid, we used the tartrazine *O* (*C.I.* 640, from G. T. Gurr, London, S.W.6). With the tartrazine counterstaining the colour of the granules of the mast cells of the lizard, the carp and the viviparous toothcarps turned from fuchsia-red to brick-orange, whereas the other substances giving a positive periodic acid – Schiff reaction remained completely unchanged.

The night-blue method and the tartrazine counterstaining described appear to be excellent techniques also for the mast cells of the lizard, the carp and the viviparous toothcarps. The clarity of the two staining methods greatly facilitates quantitative routine estimation of the mastocyte content of tissues in lower vertebrates.

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BIOLOGY

Perception of Distance in Animal Echo-Location

In a recent article[1] Nordmark fails to explain two features of the bat's ultrasonic transmissions ; one is the frequency sweep used by most species of bat employing echo-location as a means of orientation, and the other is the apparent difference between Vespertilionidae and Rhinolophidae which in fact has been shown to be a similarity[2]. As with all hypotheses related to the behaviour of animals none can be proved beyond doubt, nor can we expect any to be complete; we may, however, assume reasonable efficiency in the use of the information contained in echoes received by the bat as it relies on such information for its very livelihood.

The means, suggested by Nordmark, whereby the bat locates objects in space by listening to the note produced by two pulses arriving at the ear in quick succession is only a second-order effect (the response of the ear to the fundamental of the wave envelope is

very small compared with that from the higher frequency wave), and it is unlikely that it is used directly. The bat would find no benefit from the frequency-sweep within the pulse, first observed by Griffin[3], if it used this method. Analysis of some of Griffin's records on an instantaneous spectrum analyser show the frequency modulation sweep to be nearly linear. Such a frequency sweep can provide very much more information than the simple pulse method although it is much more difficult to explain adequately[4]; and since Rhinolophidae also employ a frequency-sweep at the end of the tone transmission, it seems reasonable to believe this to be an important feature of the bat's echo-location system.

I have recently carried out some experiments in connexion with a blind guidance device which have served to confirm my beliefs. Both a pulse and a frequency-modulation echo-location system were tried on several subjects who had no knowledge whatsoever of the systems being tested or of the results to expect, so that they could only judge by their direct observations. Both systems used the same ultrasonic transducers which were capable of operating over a frequency band of 20 kc./s. centred on 50 kc./s. The transmitted energy was sufficient to render background noise insignificant at the ranges used in the tests. The pulse system employed pulses of 50 kc./s. tone lasting from between 0·1 msec. to 15 msec. which could be chosen in 5 steps and the signals presented to the ear were pulses of 3 kc./s. tone approximately. The maximum distance to an object was 15 ft., and therefore the transmission and echo overlapped in some of the tests. A 9-in. diameter metal sphere was detected at up to 10 ft. but the distance could not be determined except by the amplitude of the echo, and this with very little certainty. In some tests the transmission could not be heard by the observer; in those where it could the intensity was comparable with the largest echo experienced. Nevertheless there was little difference in the poor ability of the subject to locate an object as a result of this.

The frequency-modulation system on the other hand used a transmission which varied linearly from 60 kc./s. to 40 kc./s. at a rate which produced a difference frequency of 3 kc./s. between transmission and an echo from 15 ft. Thus the subject experienced signals covering a frequency-range of 0–3 kc./s. depending on the distance to the object. Using this system there was no difficulty in determining the distance to an object, depending only on the ability of the subject to estimate the frequency; for example, an object at 10 ft. would produce an echo at the subject's ear corresponding to an interrupted 2 kc./s. tone. With such a system even fine wires of only 1 mm. diameter could be detected with reasonable ease. This was quite impossible with the pulse system.

The conclusion drawn from these tests was that the effect described by Nordmark is very weak compared with what can possibly be obtained from the frequency-modulation sweep. Pye has shown how such a system is possible physiologically in the bat and therefore more likely to be used[2].

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The theory of range perception in animal echo-location, recently advanced by Nordmark[1], was of great interest as I had just published a theory for bats which also depends on a frequency analysis[2].

Dr. Nordmark refers to the work of Thurlow and Small[3], who describe a time-difference tone which is heard by man when pairs of sound pulses are repeated at rates greater than 25/s. The frequency of this tone is inversely proportional to the shorter pulse-separation time, and Thurlow and Small obtained some evidence that it is a central effect, produced as a measure of the interval between two sets of sensory nerve impulses. This phenomenon thus appears to provide evidence for a central timing mechanism, originally proposed for bats by Hartridge[4] and which I had found difficult to visualize.

However, any central mechanism must be limited for very short time-intervals by the refractory period of the sensory nerve. In support of this, Thurlow and Small found that for two pulses of equal intensity the minimum interval which produced a time-difference tone was about 1 msec.; shorter intervals were only effective if a small pulse preceded a larger one[3], an improbable situation in echo-location. If the second pulse were decreased in intensity (or the first one increased) this period was progressively lengthened. Grinnell and Griffin[5] have shown that the bat's auditory system can resolve pairs of equal pulses down to a separation of 1 msec., corresponding to a very intense echo returning from 16·5 cm. But a bat feeding on flying insects, which may be taking evasive action[2], must surely be able to obtain information down to the last few centimetres.

I have therefore suggested that at close range, when the echo overlaps with the emitted pulse, the bat could obtain information from beat-notes between the two signals. The refractory period is then not involved, since different receptor cells will be excited within the cochlea. The frequency-modulated pulses of Vespertilionids will give range and directional information, while the very constant-frequency pulses of Rhinolophids will measure the Doppler shift and so indicate the relative velocity.

Möhres[6] states that accuracy of perception extends to about 50 cm. for Vespertilionids, and to at least 6·4 m. for Rhinolophids—approximately the ranges expected for beat-note operation. But Vespertilionids in flight appear to have some appreciation of objects at greater distances. Possibly location is initially achieved by the time-difference apparatus, while at close range the beat-notes are used. The latter could be much more accurate as the beat-frequency may change by 40 kc./s. over a range of 50 cm. This depends however on an equal rate of frequency change in every pulse, which has not yet been established.

The long, unmodulated pulses and low repetition-rates (less than 10/s.) of the Rhinolophids do not appear to lend themselves to time-difference measurement. Möhres has rejected such mechanisms for these bats and suggested that they obtain information from the direction and loudness of the echoes. The beat-note mechanism makes this possible by avoiding masking. The rapid vibration of the ears, by producing additional Doppler shifts, can endow them with greater directionality than their size suggests, and also allows operation under stationary conditions.

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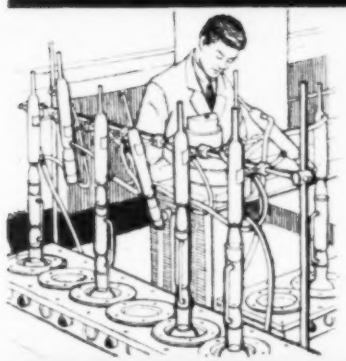

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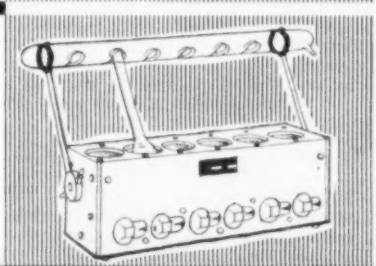

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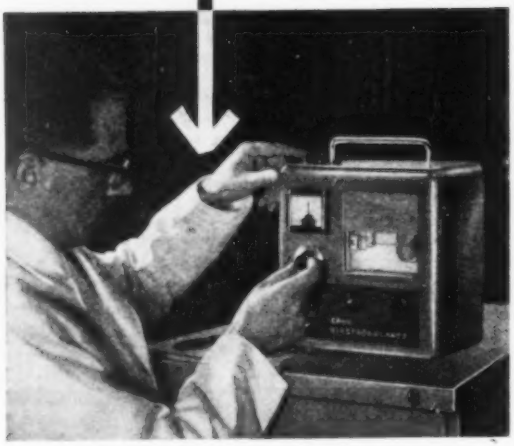

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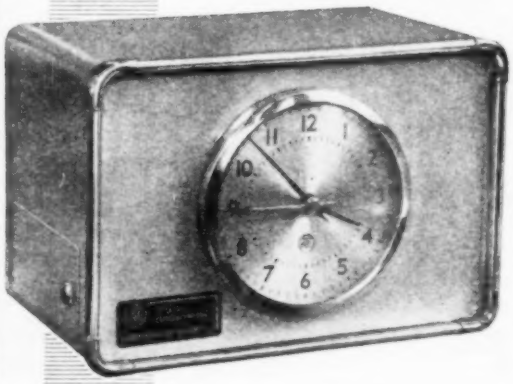

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precision in this form of echo-location. Preliminary tests show that time-difference tones are weak for the echoes of small objects, although this need not be so in bats. It seems that frequency modulation gives little, if any, improvement. Rectification (used for the detection of beat-notes) does appear to help, presumably by allowing the ear to use the pulse envelope component as well as the carrier. No time-difference tones can be produced with artificial Rhinolophid pulses.

The complex pulses of other echo-locating animals will not form useful beat-notes. Direct echo-delay measurement, by a process such as that indicated by the time-difference tone, appears to be the only possible mechanism for these cases at present. It is suggested that the interception of flying prey by insectivorous bats is related to the characteristically simple frequency structure of their pulses, which are thus potentially more informative. But as Dr. Nordmark states, it is not certain which properties of the echoes are actually used. Further investigation is necessary before these theories can be evaluated and some understanding of the true mechanisms can be achieved.

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The frequency sweep used by some bats is unlikely to be essential for distance perception by these animals, and is possibly no more than an accidental consequence of their method of sound production. When the cricothyroid muscles of the larynx of *Eptesicus* bats are denervated the modulation is altogether absent and the frequency becomes constant at about 10 kc. Yet such bats land normally on walls and avoid obstacles of moderate size. A slight decline in performance can be attributed to the greater wave-length used and the reduced vigour of the bats as a result of the surgical operation[1].

The success of these animals even under such drastically altered conditions points to the danger of attaching too much importance to specific properties of the sounds used in estimating distance. If distance is indicated by the pitch of a tone some other facts are also more difficult to explain if one assumes that the pitch is a function both of distance and definite properties of the sounds, as Kay and Pye do, rather than only of distance, as I do. If the frequency-sweep were utilized in the way these authors suggest, each animal would have to work out its own scale for measuring distance and maintain its particular sweep characteristics under all conditions. The critical variable is the rate of change of frequency, which would have to be constant. As this is a function of the frequency-range and the duration of the sweep, each of these factors must be held constant or changed to a degree which compensates exactly any change in the other factor. Such precise and complicated mechanisms for events of a few milliseconds' duration are unknown in biology. Novick[2] and Griffin[1] give many examples of the variability of the frequency-range, rate of change and duration of the sweep. Griffin's records for the bat *Eptesicus*, for example, show clearly that the decreased pulse duration as the bat approaches an obstacle results in an increased rate of change of frequency.

The typical decrease in pulse duration will also preclude the overlap between outgoing pulse and returning echo, which a frequency-modulation method of echo-location presupposes, until the last 17 cm. or so. Pye does not take this progressive decrease into consideration and it is indeed inexplicable if an overlap is to the bat's advantage. He might possibly argue that it is only during the last 17 cm., where the time-difference mechanism may fail, that the frequency sweep acquires its importance. We have to bear in mind, though, that this distance will be covered in about 1/20 of a sec., which is the reaction time between the hearing of an echo and the turning of a bat's flight according to Griffin. The interception of flying prey can be accomplished also by insectiverous bats using a different type of pulse and therefore likely, as Pye has pointed out, to use a time-difference mechanism.

The alleged advantages of the frequency-modulation method cannot be substantiated by experiments which use instruments capable of a high degree of precision for sound production and a non-linear device instead of the ear to generate the difference tones. Nor can the failure to hear a time-difference tone under certain conditions prove anything as long as we are not given the experimental details.

As Thurlow and Small had no reason to measure the thresholds for the sweep-tone under the extreme conditions—particularly the high intensity—which would correspond to animal echo-location, we cannot use their results to decide whether their pitch phenomenon is the whole answer to the problem of distance perception or not. I have recently been able to verify though, that the sweep-tone can be heard: (*a*) when the pulse-rate is irregular; (*b*) when pulses corresponding to those of other animals are present; (*c*) when the signal/echo ratio is much greater than in earlier experiments; (*d*) when the pulse-rate is no more than 2–3 per sec. and the (long) pulses overlap, corresponding to the situation for the Rhinolophidae.

Pye has raised an important point when he asks how short the interval between pulse and echo can be without abolishing the time-difference tone. The basis of this pitch phenomenon can scarcely be that suggested by Kay, and is likely to be found in the synchronized response of the nerve to pulsed stimuli. As synchrony can be maintained up to 4,000 c.p.s., the shortest interval may be 0·25 instead of 1 msec.[3]. As Dijkgraaf[4] has shown that a bat can react to a worm held about 5 cm. from the animal's mouth, the tentative limit of just over 4 cm. for the time-difference mechanism is low enough in this case.

The maximum distance recorded at which an object was detected, 6·4 m. for a Rhinolophid bat, is more difficult to explain. A pitch of 22 c.p.s. may be slightly low to serve as a reliable sign. It is important to

remember, though, that echo-locating animals probably react to change and rate of change of pitch rather than absolute pitch. Under certain conditions no sharp distinction can be made between change of pitch and change of timbre, and it may be that a slight modification of the timbre is the earliest sign in many situations. If we assume that the Rhinolophidae judge the distance by the loudness of the echo we will instead be faced with new difficulties. How, for example, can these bats judge the loudness of the echo when the interval between outgoing pulses may be as short as a few milliseconds[2] ?

It should be added that the frequency of these pulses is not quite constant and therefore unlikely to be used for estimating distance according to the Doppler principle.

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Insecticide Resistance in Mosquitoes

A DETAILED study of the nature and mode of inheritance of dieldrin-resistance in a strain of *Anopheles gambiae* from the Western Sokoto region of Northern Nigeria, and of DDT-resistance in a strain of *A. sundaicus* from Indonesia has already been made and recorded[1-3]. Dieldrin-resistance in *A. gambiae* was shown to depend on a single genetic factor semi-dominant in its manifestation and imparting cross-resistance to other cyclodiene chlorinated hydrocarbons and to γ-BHC but not to DDT. DDT-resistance in *A. sundaicus* also shows a monofactorial type of inheritance, but here the factor is recessive in nature and imparts cross-resistance to DDT-analogues but not to dieldrin or to γ-BHC.

Two other dieldrin-resistant strains of *A. gambiae* have now been studied, one from Kano in Northern Nigeria[4], and one from Bobo Dioulasso in French West Africa, and an identical type of resistance to that found in the strain from Western Sokoto demonstrated. In addition, dieldrin-resistance has been studied in three other species of mosquitoes, *A. albimanus*, *A. quadrimaculatus* and *Culex fatigans*, and a single semi-dominant factor has been shown to operate in all of them. The resemblance of the resistance in the two anopheline species to that previously investigated in *A. gambiae* is enhanced by the fact that the discriminating dosages of dieldrin separating susceptibles from hybrids, and hybrids from resistants, are almost identical in both larvæ and adult tests. In the case of *C. fatigans* the discriminating dosages applicable to the adults are somewhat higher than in the anophelines. In other words, the susceptible and hybrid adults are more tolerant to the insecticide than are the adult anophelines.

Three strains of *A. quadrimaculatus*, one from Maryland, one from Florida, and one from South Carolina, United States, have been used in these investigations. From the first two, dieldrin-resistant strains have been selected which are susceptible to DDT. Attempts to select DDT-resistance from the original mixed populations have failed. The South Carolina strain is susceptible to both insecticides.

The dieldrin-resistant strain of *C. fatigans* originates from Ceylon. Attempts to select DDT-resistance from it have so far failed. The susceptible strain of this species, used for crossing with this resistant strain, is one from Malaya. Both strains are much more tolerant to DDT in the adult stage than any susceptible anophelines. In fact they appear to be as tolerant as the DDT-resistant strains of anophelines so far investigated. However, the larvæ are more susceptible to DDT than those of susceptible strains of anophelines. It would thus appear that *C. fatigans* shows a natural high tolerance to DDT in the adult stage, and that this is a characteristic of the species and does not stem from any specific factors for resistance.

The dieldrin-resistant strain of *A. albimanus* was selected from a mixed population of this species from El Salvador. Like the other dieldrin-resistant species it is susceptible to DDT. The susceptible strain of the same species used for inheritance studies originated from Panama. Selection of the original mixed El Salvador population with DDT resulted in the production of what was apparently a true DDT-resistant strain of this species. Testing this selected strain on dieldrin revealed the presence of some dieldrin-resistant individuals, and selection of it with this insecticide produced a strain which would tolerate very high dosages of both DDT and dieldrin on consecutive exposures, that is, a strain showing double resistance.

From the strain showing DDT-resistance and some dieldrin-resistant individuals has now been isolated a strain resistant to DDT and completely susceptible to dieldrin by selection from the offspring of individual females.

This isolation of three strains of the same species, one resistant to DDT but susceptible to dieldrin, one resistant to dieldrin but susceptible to DDT, and a third resistant to both insecticides, is in itself a proof that two separate genetic factors are involved. Further confirmation has come from the crossing of the DDT-resistant strain with the susceptible Panama strain and studying the mode of inheritance of DDT-resistance. A pattern of inheritance has been demonstrated almost identical with that shown in *A. sundaicus*, namely, a monofactorial type of inheritance dependent on a virtually recessive factor. It remains now to cross the DDT-resistant strain with the dieldrin-resistant to show whether the factors occur on the same chromosome (and, if so, how far apart) or on separate chromosomes, and this work is in process.

Finally, DDT-resistance has also been studied in a third anopheline species, *A. stephensi*. By comparing a resistant strain from Iraq with a susceptible strain from India and crossing them, DDT-resistance in this species has been shown to impart cross-resistance to DDT-analogues but continued susceptibility to dieldrin and γ-BHC. The inheritance pattern differs slightly from that shown by *A. sundaicus* and *A. albimanus* in that the single factor involved is semi-dominant when 24-hr. mortalities from exposures to the insecticide are considered. When, however, immediate knockdown counts after removal from the insecticide are made, the factor appears to be more recessive than dominant.

DDT-resistance in *A. stephensi* is of a comparatively low order, some 10–20 times only, and exact discrimi-

nation between the genotypes is impossible. The establishment of the monofactorial character of the inheritance of resistance in this species has been confirmed finally by a process of repeatedly back-crossing the heterozygote with the susceptible parent and exposing the offspring to a dosage of DDT which is known to eliminate susceptibles completely. The survivors have then been re-crossed with the susceptible strain and the process of selection repeated. The mortality at each stage of selection has remained more or less at the same level. It has not shown the consistent rise expected where more than one genetic factor is involved.

These investigations, then, have amply confirmed that resistance in mosquitoes is of two independent types, DDT-resistance and dieldrin-resistance. Further, they have shown that resistance is dependent on a single genetic factor, semi-dominant in the case of dieldrin-resistance and recessive or nearly so in the case of DDT-resistance, the remarkable feature being that these characteristics apply to different species in widely separated parts of the world. That the two factors can exist together in the same population of the same species is now definitely established, and should further stimulate the search for new and efficient insecticides outside the chlorinated hydrocarbon group of organic chemicals.

The details of these experiments are being prepared for separate publication.

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Parental Care in a Rare Spider *Pellenes nigrociliatus* (L. Koch) var. *bilunulata* Simon

In May 1959, on a strongly sunlit slope of a roadside scarp adjacent to a pine wood in Toruń (northern Poland), about 20 specimens of snail shells (*Helicella candicans* (L.Rfv.) were found each of which was suspended high above the ground (up to 18 cm.) on plants (mostly grass) by means of a 'rope' twisted together from many spider-silk threads 1–3 cm. long. The entrance to the shell was closed by a 'curtain' made from thick spider's fabric. From time to time a horizontal slit (Fig. 1) opened in the curtain, and a pair of white-haired spider's pedipalps appeared in it (Fig. 2). It was, however, difficult to make the inhabitants of the shells come out of them, though they attacked fairly vigorously a needle brought close to the opening in the curtain.

The spiders were compelled to leave the shells by putting them on a warmed base. The spider inhabiting the shell (Fig. 3) proved to be a rarity. Dr. Jacques Denis (Anzin-Nord, France) identified it as *Pellenes nigrociliatus* (L. Koch) var. *bilunulata* Simon. According to him, until now this form has been known only as one specimen found in France (Tarn).

During June and July 1959, in the course of several trips, I found, on the same scarp, 20 more suspended shells of the same species. All specimens of spiders

Fig. 1. Entrance to spider's 'nest' (× c. 4·7)

found were females. They were taken to the laboratory and placed in small glass terraria, with empty snail shells on the floor—the same which abounded on the scarp. Expelled from their shells, in the same way as in the first case, they were left in the terraria. Soon it was noticed that some of the spiders were attaching threads to the empty shells. Then, in absence of plants, they attached the threads to the wall of the terrarium. After suspending the shell they entered and closed the entrance with a thick curtain of spider's web. As it appeared later, they made nests in the shells. During June–July, about 10 eggs enveloped in a very thick, silky, unusually ductile fabric were found in the particular shells. The spiders hatched underwent their first moult in the shell, and only then began to leave the shells; but for a long time they would return to them.

Fig. 2. The spider appearing in the 'nest' entrance (× c. 13)

Fig. 3. The spider on the shell (× 4)

In 1959 no male was found on the scarp. During early April 1960 the scarp was searched. At that time only the earliest plants were growing and grass was still scarce. One male spider, similar to the females found before, was seen on the ground. There were, however, no suspended shells. In May the search was repeated, and 18 suspended shells with a female in each of them and eggs in some were seen.

The spiders were taken to the laboratory, where systematic observations have been conducted on the behaviour of the adults and of the young.

I am grateful to my assistant, W. Kokociński, for the photographs.

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Flowering Behaviour of Vanilla

The vines of *Vanilla planifolia* Andrews will climb to heights of 60 ft. or more, if provided with a sufficiently tall support plant. The vine must therefore be trained to a height convenient for pollination and harvesting in the commercial production of vanilla. The prevention of the natural tendency to climb is thought to enhance the production of flowers[1]. It is believed that flowering will not occur as long as the vine can climb upward[2–7]. Childers[3] suggests that "bending of vine appears to be an important factor in causing it to flower and fruit beyond the bend, which may be due to an accumulation of carbohydrates and possibly other flower-forming materials in this region of the vine".

Observations on the flowering and fruiting of *V. planifolia* have recently been made in an abandoned vanillery in western Puerto Rico, which had not been under cultivation for at least 15 years. Since the plants in this area were growing on both short and tall supports, the plants were of both a rambling and a climbing habit of growth. Both types were inspected for flowering. Five plants of the low-growing type gave a total of 65 inflorescences on horizontal and descending branches, while no evidence of flowering was observed on the few short ascending stems present. Ten vigorous, climbing plants were selected at random, and counts were made of flower spikes on ascending and descending stems. Ascending, or climbing stems had a total of 82 inflorescences, while descending stems had a total of 29 flower spikes. One plant with 18 flower spikes consisted entirely of two main branches which had grown to a height of 60 ft. and were still climbing. The majority of inflorescences occurring on ascending vines were 30–50 ft. above the ground, and were on stems that were free of bends for at least 10 ft. in either direction. The absence of flowers on the lower 30 ft. of the climbing plants suggests that a considerable amount of growth may be necessary before flowering occurs, and that flowers should not be expected to occur on the short basal stems of rambling plants.

The inflorescences on ascending vines were capable of bearing fruit, and on one plant with 27 pods all occurred on climbing stems.

These observations indicate that *Vanilla* will flower and set fruit, whether climbing or not, and that a change in the direction of growth is not necessary for flower formation.

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Striate Mosaic: a New Disease of Sugar Cane

The term 'striate mosaic' is proposed for a new disease of sugar cane found in the varieties Pindar and Q.57 in the Lower Burdekin district in north Queensland. The most obvious features are the short, fine striations which can just be separated by the naked eye. They are a lighter colour than the normal leaf blade and show first on the youngest exposed leaf and reach their best development as the leaf expands, but are difficult or impossible to find on mature and older leaves. They occur less in the region of the large vascular bundles than in the tissue between and so in the aggregate often give a marked striping effect on the younger leaves, or even a yellowing to the entire top. Severe stunting is usually associated with the striations but striations without obvious stunting have been found in Pindar.

The disease is sett-transmitted and heat treatment of the setts in water at 50° C. for 3 hr. or in air at 54° C. for 16 hr. (as used in the control of ratoon stunting disease[1]) failed to free them from the disease. Inoculations into healthy setts did not produce the disease but the striations alone or with the stunting may be transmitted by the Soin inoculation technique[2]. It spreads very slowly in the field, and the use of disease-free planting material should prevent it ever causing serious losses.

It would appear that viruses, one causing the striations and one the stunting, are responsible for the disease.

A detailed report is in course of preparation.

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Moisture Conditions for testing Germination

THE International Standards for Seed Testing[1] detail the requirements for assessing the viability of many species, but provide only general directions for the moisture regime to be used, namely, "For most kinds of seeds, blotters or other paper substrata should not be so wet that by pressing, a film of water forms round the finger". In soil physics terminology, these substrata would be at an indefinite suction approaching zero (that is, free water). Furthermore, the suction is not necessarily constant throughout the test, namely, "subsequent watering if any should be left to the analyst".

We have adapted simple experimental equipment[2] to determine the influence of small changes of suction at or about zero suction. Representative replicated results for three species under identical illumination, temperature, and relative humidity environments are listed in Table 1. Seeds were selected for uniformity and dusted with tetrachloro-*p*-benzoquinone to prevent fungal growth. Germination was taken as being the emergence of the radicle, instead of the "emergence and development from the seed embryo of the essential structures which for the kind of seed are indicative of its ability to develop into a normal plant under favourable conditions"[1]. If this latter definition had been used, the differences between suctions would have been more marked, since the faster germinating seeds also showed faster development; for example, after 18 hr., oats at 0 cm. suction had 1 cm. green shoots, while at 10 cm. water suction there was only an emerged radicle, these two conditions not being differentiated in Table 1.

For each of the species described in the table, and over this limited suction-range, the total number germinated after 10 days was constant. Hence the total of the four replicates at each time has been expressed as a percentage of the total final count for that species.

Table 1. CUMULATIVE GERMINATION EXPRESSED AS PERCENTAGE OF THE NUMBER OF VIABLE SEEDS OBTAINED AFTER 10 DAYS OF TREATMENT

Species	Suction cm. of water	Days of treatment 1	1½	2	2½	3	5
Avena sativa L. var. Klein (oats)	0	0	0	30	51	80	98
	2	0	0	2	15	57	93
	4	0	0	2	3	33	92
	6, 8 and 10	0	0	0	2	21	82
Medicago sativa L. (lucerne)	0	90	93	96	97	98	99
	2	70	83	96	97	98	99
	4	67	83	96	97	98	99
	6, 8 and 10	61	77	96	97	98	99
Lolium perenne L. Mansfield strain (perennial rye-grass)	0	0	0	24	39	69	95
	2	0	0	35	51	84	97
	4	0	0	37	53	91	99
	6, 8 and 10	0	0	39	65	93	99

Both oats and lucerne show a significant decrease in germination-rate on increasing the suction from 0 to 6 cm. water, while perennial rye grass showed an increase in rate over the same range.

These germination results were compared with those from the New South Wales State Department of Agriculture Seed Testing Laboratory using the same seed sample and the procedure of the International Rules[1]. The final count numbers at 10 days were identical, but the rates for 'standard' treatments varied more than those of all the suction regimes listed in Table 1. This variation can therefore be attributed to inconstancy in the moisture regime of the substrata, which under the existing standards is outside the control of the tester. In those laboratories, where seed testing is infrequent, it is likely that variability will be greater than in routine testing, particularly when attempting to obtain comparable moisture conditions for seeds differing in size and shape.

It is suggested that small variations in moisture regime have been the cause of inconsistencies attributed to other factors; for example, Ahring *et al.*[3] investigated temperature differentials encountered in seed germination experiments, but as the moisture regime was not specifically controlled (it would require some form of tensiometer to detect small differences within the range 0–6 cm. water) all the detected responses cannot be attributed to a temperature factor.

Isely[4] recommends placing the Petri dishes of substrate within plastic freezer bags containing wet filter papers to saturate the atmosphere. However, this would not easily maintain any particular suction and would only minimize loss of vapour. If seeds were to be germinated on tension plates, a suction for optimal germination could be specified for each species, hence eliminating the use of various types of substrata.

Acknowledgement is made to Miss Amy Meyers of the New South Wales State Department of Agriculture Seed Testing Service for her help.

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ENTOMOLOGY

Termination of Diapause in *Acheta* by Urea

THE rate of termination of diapause in eggs of *Acheta commodus* (Walk) has a negative temperature coefficient within the range −16·5 to +5° C.[1]. It has been reported by Jacobsen and Christensen[2] that the initial stages of denaturation of β-lactoglobulin by urea has a negative temperature coefficient. Accordingly, experiments have been carried out with certain denaturants, primarily urea, for evidence of any effect on diapause. The attempt was made to incorporate the chemicals into the eggs by making use of the capacity of Orthopteran eggs to take up water during their development. In *Acheta* the uptake of water occurs slightly later than the onset of diapause[3].

(1) Eggs, up to one day old, were placed on blotting paper disks previously moistened with solutions of the chemicals under test. They were then incubated, in sealed tubes, at 27 (± 0·2)° C.

Definite responses were obtained with urea. Table 1 shows that urea solutions at the strengths normally used for denaturation of protein were extremely toxic but at a concentration of 0·08 *M*, a highly significant increase occurred in the proportion of eggs that completed their development without evidence of diapause.

Table 1. Percentage of Eggs developing without Evidence of Diapause after Exposure during the Pre-diapause Stages to Solutions of Urea at the Concentrations Indicated

Molar concentration	0	0·02	0·04	0·08	0·0
Percentage hatch	6·7	5·3	8·3	31·7	0
Percentage mortality	5·3	0	4·0	32·0	100

(2) The capacity of urea to increase the rate of termination of diapause was revealed in the following experiment. Pre-diapause eggs were treated with urea at a concentration, 0·02 *M*, insufficient to eliminate diapause in eggs held at 27° C. When held at this temperature, 95 per cent of the eggs, both treated and controls, entered diapause.

Incubation was continued at 27° C. until the completion of hatching. The median duration of exposure (period for 50 per cent hatch) was 35 days for the eggs treated with urea, in comparison with 54 days for the control.

Evidence to be described elsewhere shows urea to be absorbed into the egg.

The low concentration of urea in the above experiments would seem to make it unlikely that denaturation takes place. Nevertheless, relatively mild agents can cause reactions of this type, such as sulphydryl – disulphide exchange[4], or disturbance of the protein hydration structure (ref. 5 and personal communication). Although no reactions to concentrations as low as those reported here have been described, the possibility of steric effects must be considered.

A more detailed report of these and other experiments will be published elsewhere.

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The Prothoracic Gland and Colour Change in Locusts

Many locust species are characterized by large variations in colour, morphometrics and behaviour, variations which are related, under natural conditions, to the density of the population[1]. When numbers are high the nymphs, or hoppers, live in dense bands, and these gregarious hoppers are orange or yellow and black in colour. When populations are low the hoppers do not group together, and such solitary locusts are fawn or green, with only small amounts of darker pattern. In the laboratory, gregarious locusts may be produced by rearing the hoppers in crowds, and solitary locusts by rearing each individual in a separate cage, out of visual and tactile contact with others[2]. The behaviour of locusts changes rapidly, according to the number of contacts that hoppers make with each other[3]. Changes in colour and in morphometrics require more continuous contact (or lack of contact) with other locusts[4,5]. It has been suggested that the colour changes are controlled, at least in part, by hormones, and that the hormonal balance of solitaries differs from that of gregarious individuals[5,6].

During an endocrinological investigation of two species of locusts, *Locusta migratoria migratorioides* (R. and F.) and *Schistocerca gregaria* (Forsk.), we observed that the prothoracic gland (ventral gland) is shaped differently and significantly larger in solitary than in gregarious individuals (Fig. 1). The corpus allatum was also slightly larger in solitary individuals, while there was no apparent difference in the size of the corpus cardiacum. The larger size of the prothoracic gland in solitary individuals suggested the experiment of extirpating part of this glandular tissue, leaving *in situ* an amount approximately equal to that found in gregarious animals. The results of preliminary experiments of this kind, performed on nine pairs of *Schistocerca* hoppers, have substantiated the validity of this approach to the problem of colour change in locust phases. The hoppers were reared in isolation from hatching and throughout the course of the experiment. Soon after the moult to the fourth instar, hoppers were matched in pairs of the same sex and coloration. In one of each pair, three-quarters of the prothoracic gland on one side was then removed. The other animal of the pair was subjected to a blank operation and served as a control. Before the operation the animals were green in colour, with varying small amounts of blackish-brown pattern. After the moult, to the fifth instar, the hoppers that had been deprived of a portion of the prothoracic gland had developed extensive areas of black pigmentation, similar to that of gregarious hoppers, while the background colour had changed from green to yellow or creamy-pink, similar to that found in gregarious hoppers, or in those which are becoming gregarious[4]. The

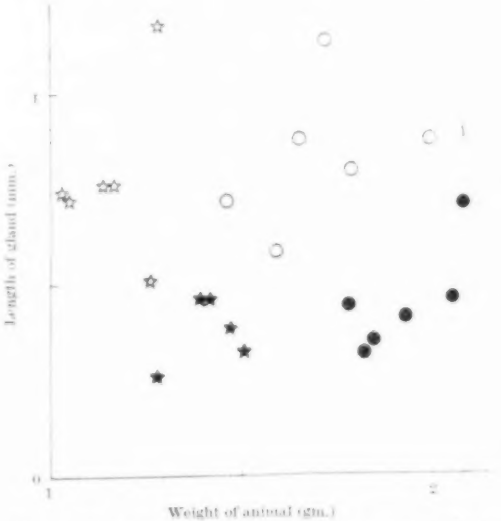

Fig. 1. The size (greatest antero-posterior measurement) of the prothoracic gland in solitary and gregarious adults of *Schistocerca gregaria* killed within 6 hr. of fledging. Open symbols, solitary animals; solid black symbols, gregarious animals; stars, males; circles, females

control hoppers remained green in colour with only small amounts of black pattern.

These results seem to provide evidence that secretions of the prothoracic gland play a part in governing the metabolism of the pigments and, in balance with other hormones, in controlling changes in colour from the solitary to the gregarious phase in locusts. Further work is in progress relating to the possible role of hormone balance in other aspects of locust biology, especially behaviour.

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Experimental Hybridization of *Aedes* (*Stegomyia*) *aegypti* (L.) with *A.* (*S.*) *simpsoni* (Theobald)

HYBRIDIZATION between *Aedes* (*Stegomyia*) *aegypti* (L.) and the morphologically very distinct[1] *A.* (*S.*) *albopictus* Skuse has been a source of keen controversy since the initial work of Toumanoff[2] and Hoang Tich Try[3]. These results and those of Downs and Baker[4] and Bonnet[5] have been fully discussed by Kitzmiller[6] and Mattingly[1]. Offspring were only obtained in one direction in each case, though the successful direction varied with the strains used. Inheritance was completely maternal in the F_1 and subsequent generations with the exception of two single individuals of paternal resemblance. Suggested explanations involve sperm-entry induced parthenogenesis[4], cytoplasmic inheritance[2] and chromosomal mechanisms[1]. Recently, Woodhill[6] has repeated the crosses on a much larger scale with stringent precautions to avoid contamination. From nearly 50,000 eggs only a single adult was obtained, intermediate in characters between the two parents, indicating a certain degree of chromosomal compatibility.

A. (*S.*) *simpsoni* (Theobald) is morphologically much closer to *A. aegypti* than is *A. albopictus*, widespread in the Ethiopian region, frequently occurring together with *A. aegypti* and an important vector of yellow fever; it is nevertheless of distinct habits, breeding almost exclusively in plant axils while *A. aegypti* does so only rarely. *A. simpsoni* used in the present work were the F_1 from wild-laid eggs collected at Ganda, Kenya, by members of the Medical Department, to whom I am indebted. The adults reared in London were hand-mated[3] (normal mating does not occur under usual laboratory conditions); 8 out of 10 mated females oviposited normally and 7 of the egg batches were fully fertile. The *A. aegypti* used were a heterogeneous F_2 from larvæ collected at Port Swettenham, Malaya, through the kindness of Dr. R. H. Wharton of Kuala Lumpur. Mostly var. *queenslandensis*[10], they were largely heterozygous for the genes for white abdomen[11] and white-spot[12] and mated naturally in $\frac{1}{2}$-pint paper cups.

In making the crosses the females were first given a blood meal and then hand-mated[3] with males of the other species. The mated females were confined in a 3 × 1 in. tube over a moist pad on which they oviposited. Hatching was effected by adding deoxygenated water to these tubes.

18 out of 19 female *A. simpsoni* mated with male *A. aegypti* laid egg batches, from 4 of which 9 larvæ hatched. 7 out of 17 female *A. aegypti* of the reciprocal mating laid egg batches, none of which hatched, 3 of the larvæ died before reaching the 4th instar; the remainder, from 3 different matings, were reared to give 2 identical adult males and 4 identical adult females in perfect condition. A male and female are illustrated in Fig. 1 together with examples of the parental species.

These hybrids have some characters typical of one parent and some of the other, with a few intermediate between the two. Characters typical of the maternal parent *A. simpsoni* include the spines at the base of the thoracic tufts of the 4th-stage larvæ, absence of any scales on the clypeus, the anterior scutal spot large and broad-scaled and the supra-alar spot large.

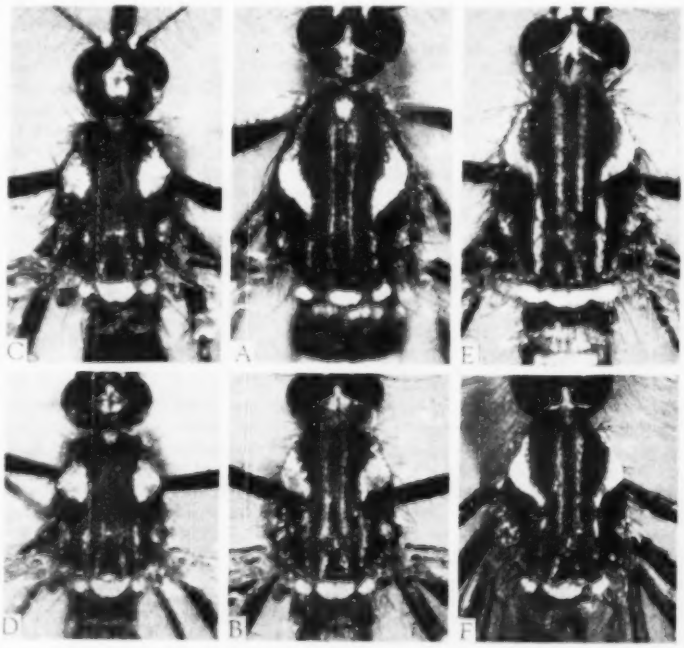

Fig. 1. A hybrid between the mosquitoes *Aedes* (*Stegomyia*) *aegypti* (L.) and *A.* (*S.*) *simpsoni* (Theobald). The thoraces of *A.* ♀ hybrid; *B*, ♂ hybrid; *C*, ♀ and *D*, ♂ maternal species *A. simpsoni*; *E*, ♀ and *F*, ♂ paternal species *A. aegypti*

Characters typical of *A. aegypti* include the median paired yellow lines on the scutum, the front femora with anterior pale stripes on the basal halves and the mid femora with anterior pale stripes and no median spots. Intermediate characters include the larval pecten-spines which have large basal denticles as in *A. aegypti* but are bilaterally symmetrical; the antero-lateral scutal spots are a compromise between ovoid in *A. simpsoni* and crescentic in *A. aegypti* (Fig. 1), the 4th hind tarsal, pale on the basal two-thirds in *A. aegypti* and entirely dark in *A. simpsoni*, is pale on the basal one-third.

These hybrids represent about 1 per cent of the eggs laid in the particular cross, compared with not more than about 0·06 per cent in the case of Woodhill's hybrid[8]. This seems reasonable in view of the closer affinity between the species in the present instance, although it is possible that hand-mating may result in better insemination than natural mating. The uniformity among the 4 female and 2 male hybrids suggests that chromosomal combination, though rare, is constant in its effect. The absence of offspring in the reciprocal cross must remain inconclusive until more successful matings have been made. The results support Woodhill's[8] suggestion that the earlier results with *A. albopictus* might be due to contamination by stray eggs. True hybridization when it occurs between *Stegomyia* species probably results in a blending inheritance with a frequency of occurrence indicative of the extent of evolutionary divergence within the subgenus.

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VIROLOGY

Use of a 'Mixed Hæmadsorption' Method in Virus-infected Tissue Cultures

The principle of mixed agglutination[1] has been used by Högman[2] to indicate the presence of blood-group antigens in tissue culture. In this system the cultured cells are sensitized with antibodies directed towards antigens of the cell surface. Thereby the cells acquire capacity to adsorb homologous red cells. Vogel and Shelokov[3] have shown that certain viruses can be located in tissue cultures by their capacity to adsorb sensitive erythrocytes, the so-called hæmadsorption test. Two pre-requisites for this system are: (1) that virus antigen be available on the surface of the infected tissue cells; (2) that this antigen fix the erythrocytes.

This communication outlines some attempts to apply a similar system to indicate virus antigens present on tissue culture cell surfaces, but which do not fix red cells spontaneously. Initially cells infected with vaccinia virus were chosen as an experimental model because viral antigen located on the cell surface is assumed to exist (spontaneous hæmadsorption with chicken erythrocytes). The sheep red cells used in the present experiments are not spontaneously adsorbed on vaccinia-infected cells unless treated as described here.

Table 1. 'Mixed Hæmadsorption' in Vaccinia Virus-Infected Tissue Cultures treated with Different Concentrations of Anti-vaccinia Rat Serum.

Positive hæmadsorption graded as + + +, + + or +; − indicates no hæmadsorption

	Indicator cells	Dilution of rat serum added to the tubes					
		Anti-vaccinia serum					Normal rat serum
		10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}	10^{-2}
Vaccinia virus-infected tubes	Positive cells	+ + +	+ +	+	(+)	−	−
	Negative cells	−					
Normal tube	Positive cells	−					

Positive cells, tanned sheep erythrocytes coated with 100 γ/ml. rat globulin and rabbit anti-rat serum 1/1,000. Negative cells, as above except anti-rat serum substituted for normal rabbit serum diluted /1,000.

Viral antibodies obtained from either rats or rabbits were fixed to virus-infected tissue culture cells and detected by the addition of sheep red cells coated with antiserum to either rat or rabbit sera, depending on the source of the viral antibodies.

The vaccinia virus was grown in monolayer cultures of monkey kidney tissue. Tubes with moderate virus degeneration were washed three times with the culture medium used (usually 0·5 per cent lactalbumin hydrolysate buffered with Hanks solution) and drained. Then 0·2 ml. of rabbit or rat antivaccinia serum was added in different dilutions to the virus cultures (Table 1). The tubes were kept at room temperature for 1 hr. in a slightly inclined position (about 10°) and were then carefully washed three times. Following this, the indicating system, sheep red cells coated with the specific anti-γ-globulin serum on their surface, were added to the tubes. It was established that if antibodies were fixed to the tissue culture, then, the red cells would agglutinate around the tissue cells as shown in Fig. 1.

The specific species antiserum, prepared in horse (anti-rabbit serum) or rabbit (anti-rat serum), can be fixed to the sheep red cells in two ways. One method consists of coating tanned sheep cells[4] with, for example, rat γ-globulin 50–100 γ/ml. Rabbit anti-rat serum was then allowed to combine with the coated sheep cells in a dilution of the serum (1/1,000) that produced agglutinates of moderate size.

The other method differs only in that the sheep cells were not tanned, but were sensitized with rabbit immune (anti-sheep) serum, and then allowed to combine with anti-rabbit sera, of which a suitable dilution was also chosen.

The result of a representative experiment with vaccinia virus-infected cultures is shown in Table 1. It can be seen that anti-viral serum when added to vaccinia-infected cultures in dilutions up to 1/10,000 will absorb 'positive' red cells. (The HI-titre of this serum measured in the conventional way against

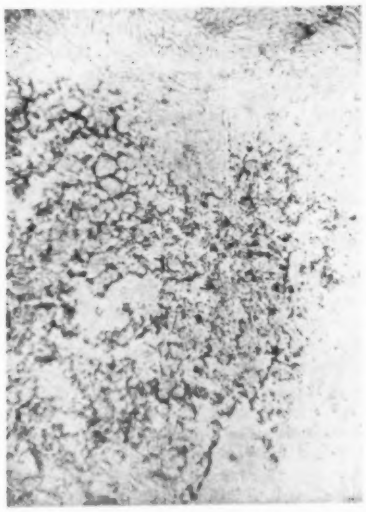

Fig. 1. Photomicrograph showing positive 'mixed hæmadsorption' on a vaccinia virus degeneration focus. Tissue culture from the experiment summarized in Table 1

4 units of vaccinia hæmagglutinin was 1/512, and the 50 per cent plaque neutralizing titre was about 1/3,000). The specificity of the system is indicated by the negative outcome of the controls given in Table 1.

Experiments have shown that essentially the same results are obtained in the vaccinia virus system when the indicating cells are prepared according to the second method, that is, sheep erythrocytes covered with, for example, rabbit anti-sheep serum and followed by anti-rabbit serum.

This latter system has also been tried with success in tissue cultures infected with measles or canine distemper virus as shown in Table 2.

The hæmadsorption on virus-infected foci was massive, and clearly visible macroscopically. When viewed microscopically, it was found that the red cells clump on the edges of the infected cells. In addition, when a very strong hæmadsorption occurred, the red cells covered the entire cell surface, presumably because the binding was strong enough to prevent the red cells from being washed away.

Attempts have been made to use this method of detection for other virus – tissue culture systems, such as those of polio and herpes simplex, but the results have been negative to date. This may be due to a difference in the release of the viruses from the infected cells as compared with that of the vaccinia and distemper viruses.

Table 2.* 'MIXED HÆMADSORPTION' IN TISSUE CULTURES INFECTED WITH CANINE DISTEMPER VIRUS. HÆMADSORPTION GRADED AS IN TABLE 1

	Indicator cells	Rabbit serum added to tubes : Anti-distemper serum dilution 1/5	Normal serum dilution 1/5
Distemper virus infected tubes	Positive cells	+ + +	–
	Negative cells	–	–
Normal tubes	Positive cells	–	–
	Negative cells	–	–

Positive cells, washed sheep red cells coated with rabbit amboceptor (anti-sheep erythrocyte serum produced in rabbit) diluted 1/1,000 and with horse anti-rabbit serum diluted 1/500. Negative cells, as above, but anti-rabbit serum substituted for normal horse serum 1/500.

* This experiment was performed in co-operation with Dr. Erling Norrby.

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New Herbaceous Test-Plants for Study of the Infectious Degeneration of Grape Vines

RECENT progress achieved in the transmission of the virus diseases of the grape vine to herbaceous test-plants, induces us to disclose further results[1].

In a series of inoculations made on 1,026 plants, of 48 different species, using various techniques, positive results were obtained in the following tests: (1) by mechanical inoculation of sap, (*a*) on *Impatiens holstani* (*I. holstii* × *I. sultani*) (one plant out of 48 of which 17 were in artificial light and 31 in greenhouse; experiments made during various periods of the year) with leaves of the clone of grape vine Alfa 7.A., (*b*) on alfalfa (two plants out of six) with roots of the clone 34*C*/59; (2) by chip-budding from young shoots, (*a*) on *I. holstani* (one plant out of 18) with the clone 101*P*, (*b*) on *Lycopersicum esculentum* (4 plants out of 30) with the clone 16*C*/59, (*c*) on the hybrid *L. esculentum* × *L. pimpinellifolium* (7 plants out of 13), with the clone 1*C*/59; (3) by dodder, on *Ammi majus* (10 plants out of 19) in five experiments made from February to June, with the clones of grape vine 3*CA*/59, *V1F22V1*, and 101*P*.

For the transmission, material was used from 32 different clones of diseased grape vines. Results were positive with only seven of them, coming from three different districts and showing at the same time malformation of the shoots and of the leaves, mosaic and yellow mosaic. These are the only symptoms noticed so far in Italy on the 'infectious degeneration' of the grape vine.

The following are the symptoms observed on the herbaceous test plants: *I. holstani*—severe malformation and twisting of the leaves, accompanied by mosaic and yellow streaks (after 4 months, by sap inoculation and after 3 months, by chip-budding); Alfalfa—mild mosaic or yellowish spots with sharp or indefinite edges on the leaves (after about 30 days); *L. esculentum* and *L. esculentum* × *L. pimpinellifolium*—vein-clearing and leaf malformation (after 30–50 days); *A. majus*—malformation and twisting of the leaves with light green or necrotic patterns along the margin (after 10–30 days).

We deduced that viruses were transmitted from the vine to herbaceous plants since: (*a*) with *I. holstani*, although the percentage of infections is very slow, we had the same symptoms using two different methods of transmission and working during different periods of the year; (*b*) with *A. majus* the percentage of infection is quite high, and, moreover, we had the transmission, only by dodder, on the same species (after 17 days); (*c*) the same clone of grape vine gave positive results on *A. majus* and *I. holstani*; (*d*) transmission made in different periods

of the year gave the same symptoms; (*e*) on *L. esculentum* × *L. pimpinellifolium* the symptoms were identical both in the inoculation from the vine and from diseased *I. holstani*.

From *I. holstani* the isolate has so far been transmitted to tobacco (varieties White Burley and Samsun) and to *Petunia*, by sap and by *Myzodes persicae*; to *Nicotiana glutinosa*, *Datura stramonium*, *Vigna sinensis* and *I. holstani* by sap. The percentage infection in the transmission from these species to the same species or to the other species that gave positive results in the inoculation from *I. holstani*, is higher than in the transmission from *I. holstani*.

We are trying to transmit the isolates from the herbaceous plants to grape vine. For this work we use symptomless grape vines, selected during three years and belonging to varieties that appeared to be very receptive to the 'infectious degeneration' in previous experiments on transmission by grafting from vine to vine.

Other work in progress is the identification of the isolates.

No rod-shaped virus particles were seen in a series of observations, using the electron microscope, with exudates obtained by Johnson's method and with drops prepared with Brandes's dipping method both with diseased grape vines (leaves, shoots and roots) and with infected herbaceous plants.

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GENETICS

Gene Action in the *X*-chromosome of the Mouse (*Mus musculus* L.)

Ohno and Hauschka[1] showed that in female mice one chromosome of mammary carcinoma cells and of normal diploid cells of the ovary, mammary gland and liver was heteropyknotic. They interpreted this chromosome as an *X*-chromosome and suggested that the so-called sex chromatin was composed of one heteropyknotic *X*-chromosome. They left open the question whether the heteropyknosis was shown by the paternal *X*-chromosome only, or the chromosome from either parent indifferently.

The present communication suggests that the evidence of mouse genetics indicates: (1) that the heteropyknotic *X*-chromosome can be either paternal or maternal in origin, in different cells of the same animal; (2) that it is genetically inactivated.

The evidence has two main parts. First, the normal phenotype of *XO* females in the mouse[2] shows that only one active *X*-chromosome is necessary for normal development, including sexual development. The second piece of evidence concerns the mosaic phenotype of female mice heterozygous for some sex-linked mutants. All sex-linked mutants so far known affecting coat colour cause a 'mottled' or 'dappled' phenotype, with patches of normal and mutant colour, in females heterozygous for them. At least six mutations to genes of this type have been reported, under the names mottled[3,4], brindled[2], tortoiseshell[5], dappled[6], and 26*K*[2]. They have been thought to be allelic with one another, but since no fertile males can be obtained from any except, in rare cases, brindled, direct tests of allelism have usually not been possible. In addition, a similar phenotype, described as 'variegated', is seen in females heterozygous for coat colour mutants translocated on to the *X*-chromosome[7,8].

It is here suggested that this mosaic phenotype is due to the inactivation of one or other *X*-chromosome early in embryonic development. If this is true, pigment cells descended from cells in which the chromosome carrying the mutant gene was inactivated will give rise to a normal-coloured patch and those in which the chromosome carrying the normal gene was inactivated will give rise to a mutant-coloured patch. There may be patches of intermediate colour due to cell-mingling in development. The stripes of the coat of female mice heterozygous for the gene tabby, *Ta*, which affects hair structure, would have a similar type of origin. Falconer[9] reported that the black regions of the coat of heterozygotes had a hair structure resembling that of the *Ta* hemizygotes and homozygotes, while the agouti regions had a normal structure.

Thus this hypothesis predicts that for all sex-linked genes of the mouse in which the phenotype is due to localized gene action the heterozygote will have a mosaic appearance, and that there will be a similar effect when autosomal genes are translocated to the *X*-chromosome. When the phenotype is not due to localized gene action various types of result are possible. Unless the gene action is restricted to the descendants of a very small number of cells at the time of inactivation, these original cells will, except in very rare instances, include both types. Therefore, the phenotype may be intermediate between the normal and hemizygote types, or the presence of any normal cells may be enough to ensure a normal phenotype, or the observed expression may vary as the proportion of normal and mutant cells varies, leading to incomplete penetrance in heterozygotes. The gene bent-tail, *Bn* [10], may fit into this category, having 95 per cent penetrance and variable expression in heterozygotes. Jimpy, *jp*, is recessive, suggesting that the presence of some normal cells is enough to ensure a normal phenotype, but Phillips[11] reported one anomalous female which showed the jimpy phenotype. Since it showed the heterozygous phenotype for *Ta* this animal cannot be interpreted as an *XO* female; it is possible that it represents an example of the rare instance when by chance all the cells responsible for the jimpy phenotype had the normal gene inactivated.

The genetic evidence does not indicate at what stage of embryonic development the inactivation of one *X*-chromosome occurs. In embryos of the cat, monkey and man sex-chromatin is first found in nuclei of the late blastocyst stage[12,13]. Inactivation of one *X* at a similar stage of the mouse embryo would be compatible with the observations. Since an *XO* female is normally fertile it is not necessary to postulate that both *X*-chromosomes remain functional until the formation of the gonads.

The sex-chromatin is thought to be formed from one *X*-chromosome also in the rat, *Rattus norvegicus*[14], and in the opossum, *Didelphis virginiana*[15]. If this should prove to be the case in all mammals, then all female mammals heterozygous for sex-linked mutant genes would be expected to show the same phenomena

as those in the mouse. The coat of the tortoiseshell cat, being a mosaic of the black and yellow colours of the two homozygous types, fulfils this expectation.

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Genetic Basis for Graft-against-Host Immunological Reactions between Two Inbred Lines of Chickens

It has been established that the enlargement of the embryonic spleen which follows the injection of adult chicken blood into chick embryos is due, at least in part, to a proliferation of cells derived from the injected blood[1,2]. Cock and Simonsen[3] have shown that virtually no splenic enlargement occurs when the blood-donor and embryonic recipients are members of the same inbred line of chickens. The phenomenon of splenic enlargement seems to be fundamentally immunological in nature, and due to donor cells proliferating in response to those host antigens which differ from any in the donor.

It should be possible, by injecting blood from adult birds from one parental line into F_2-generation and back-cross embryos between two inbred lines, to analyse the antigenic difference of the other parental line. Assuming that the antigens of the parental lines are dominantly determined and that they segregate in crosses between the lines in a Mendelian fashion, then a proportion of F_2-generation embryos, and of embryos of the back-cross to the parent of the blood-donating line, will be expected to lack those genes which determine antigens occurring exclusively in the non-blood-donating line. The proportion of embryos which lack these genes will be $(\frac{1}{4})^n$ in the F_2-generation and $(\frac{1}{2})^n$ in the back-cross, where n is the number of pairs of genes involved. Since splenomegaly will occur only when the recipient embryo possesses antigens foreign to the donor cells, these are also the proportions of embryos in the respective crosses which will show no splenic enlargement. All F_1 hybrids and embryos of the back-cross to the parent of the non-blood-donating line will receive the genes which determine antigens peculiar to the non-blood-donating line and all these embryos will therefore show splenic enlargement. Thus, an estimate of the value of n can be obtained by observing the proportion of F_2 and back-cross embryos which show no splenic enlargement. The genetic basis for this method is essentially similar to that used in analysing histo-compatibility differences between inbred strains of mice using tumour transplantation[4], and skin transplantation[5].

The method outlined above has been used to observe antigenic differences between the Rauscheath *C*- and *I*-inbred lines of White Leghorns[6]. Both lines have been brother-sister mated annually for more than twenty generations. Chick embryos were injected intravenously at 15 days of incubation with 0·1 ml. of citrated blood from *I*-line cocks, and killed 4 days later and their spleens weighed. The embryos injected were: *C*-line embryos, *I*-line embryos, the F_2-generation ($CI \times CI$ and $CI \times IC$), and the back-crosses ($C \times CI$ and $C \times IC$, $I \times CI$ and $I \times IC$). In designating the crosses, the male parent is stated first. Two *I*-line cocks were used as blood-donors to the F_2 and back-cross embryos and experiments with each donor were performed twice. Only a small number of *C* embryos were available for injection, but the marked splenic enlargements obtained indicate that *C* tissues are antigenic to *I* cells. A small number of *I*-line embryos injected with *I*-blood showed no splenomegaly. So far, we have had no F_1-hybrids to test, but Cock and Simonsen[3] have obtained splenic enlargement after injecting *I*-blood into newly hatched $C \times I$ chicks. The patterns of spleen weights obtained after injecting *I*-blood into F_2 and back-cross embryos were similar in each of the four experiments, and the results have been pooled in Fig. 1. The proportions of spleens in the different crosses showing no enlargement are shown in Table 1, and these results are compared with the theoretical frequencies expected for 1, 2 and 3 pairs of dominant genes determining antigens peculiar to the *C*-line. The proportions best fit the expectancy for one pair of genes, and the results suggest, therefore, that the *C*-line carries one antigen (capable of stimulating splenic enlargement) which is absent from the *I*-line. The results also fit the expectancy if the *C*-line possesses one dominantly determined antigen and one recessively determined antigen foreign to the *I*-cells. In this case, the proportion of unenlarged spleens in the F_2-generation would be 18·75 per cent (the proportion falls in a series $(\frac{3}{4})^{n_1} \times (\frac{1}{4})^n$, where n_1 is the number of pairs of recessive genes and n is the number of pairs of dominant genes). The proportion of unenlarged spleens in the back-crosses would remain unchanged. However, until we have other evidence for the

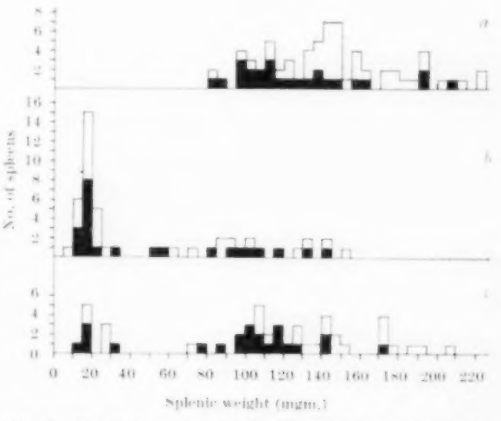

Fig. 1. Distribution of spleen weights obtained after injecting *I*-line cock-blood into F_2-generation and back-cross embryos. Solid squares, male spleens; open squares, female spleens. (*a*) $C \times CI$ and $C \times IC$ embryos; (*b*) $I \times CI$ and $I \times IC$ embryos; (*c*) $CI \times CI$ and $CI \times IC$ embryos

Table 1

Pairs of genes	Percentage of unenlarged spleens in F_1	Percentage of unenlarged spleens in F_2		Percentage of unenlarged spleens in back-crosses			
	CI	$CI \times CI$	$CI \times IC$	$I \times CI$	$I \times IC$	$C \times CI$	$C \times IC$
Experimental results	no data	20·4	$\chi^2 = 0.55$	59·2	$\chi^2 = 1.65$	0	
1	0	25	N.S.	50	N.S.	0	
2	0	6·25		25		0	
3	0	1·56		12·5		0	

Comparison between experimental segregation results and theoretical results expected for 1, 2 and 3 pairs of genes determining antigens present in C-line birds, but absent from I-line birds. The experimental data do not differ significantly from the values expected for one pair of genes.

Table 2. Differences in Mean Weights of Enlarged Spleens from Male and Female Embryos

Cross	No. of embryos	Mean splenic weight (mgm.)		Values of t (from logarithm of spleen weights)
		Male	Female	
$C \times CI$ and $C \times IC$	68	128·3	151·6	2·97 $P < 0.01$
$I \times CI$ and $I \times IC$	20	98·2	105·7	0·55 $P > 0.5$
$CI \times CI$ and $CI \times IC$	39	114·1	145·5	3·33 $P < 0.01$

occurrence of recessively determined antigens in the chicken, we are inclined to favour the former interpretation of the segregation results.

The spleens of uninjected control embryos ranged in weight from about 10 to 20 mgm. The slight enlargements (up to 35 mgm.) of some spleens which have been included in the 'no enlargement' groups in Table 1 may be attributable to the presence of additional weak antigens in the C-line. On the other hand, the slight antigenic diversity which exists within the I-line[3] must also contribute to these small enlargements.

The different patterns of distribution of the enlarged spleens in the three crosses suggest that the homozygotic or heterozygotic state of the gene determining the C antigen influences the spleen weight. That is, a gene dosage effect appears to be involved, with embryos homozygous for the C gene providing a stronger antigenic stimulus to I cells (and therefore a larger spleen) than embryos heterozygous for the gene. However, the weight of the spleen may probably not be taken as directly indicative of the homozygosity or heterozygosity of the embryo concerned, since there is evidence in two of the crosses that the sex of the recipient influences the spleen weight. The mean weights of the enlarged female spleens from $C \times CI$ and $C \times IC$ and from $CI \times CI$ and $CI \times IC$ embryos are significantly greater than the mean weights of enlarged male spleens (Fig. 1 and Table 2). The reason for this sex difference is not known: a similar effect has been observed by J. B. Solomon (personal communication). In addition to the sex and gene dosage effects, the variability in weight of the enlarged spleens will also be increased by residual antigenic diversity within both the C- and I-lines.

These results will be reported in more detail elsewhere, together with results obtained by injecting C-line blood into the C- and I-crosses. Similar analyses of differences between the C- and IC-inbred lines will also be described.

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MISCELLANY

Extra-Terrestrial Radio Transmissions

We are witness again to a surge of interest in, and speculation about, extra-terrestrial radio transmissions which had an earlier flare in the late 'twenties[1]. The favourable change in climate for the expression of such ideas since the turn of the century has been of particular interest to me. In 1899, Nikola Tesla established an experimental station at Colorado Springs, where he would be free to pursue certain electrical investigations, unrestrained by the limits imposed by his New York City laboratory. In an article by him[2], published after his return to New York in the following year, he presented a rather thrilling account of signals received while alone one night in the experimental station:

"The changes I noted were taking place periodically, and with such a clear suggestion of number and order that they were not traceable to any cause then known to me. I was familiar, of course, with such electrical disturbances as are produced by the sun, Aurora Borealis and earth currents, and I was as sure as I could be of any fact that these variations were due to none of these causes. . . . It was some time afterward when the thought flashed upon my mind that the disturbances I had observed might be due to intelligent control. . . . The feeling is constantly growing on me that I had been the first to hear the greeting of one planet to another. . . . I announced to the Red Cross Society, when it asked me to indicate one of the great possible achievements of the next hundred years, that it would probably be the confirmation and interpretation of this planetary challenge to us."

I have acquired the original of Tesla's statement to the Red Cross Society, dated Christmas (January 7), 1900, which I believe is the first expression of the possibility of radio communication with other planetary communities. The announcement was harshly criticized. This was particularly unfortunate since, because of such attacks, Tesla never produced detailed information concerning the results of his intended investigations and the chance reception of signals.

Leland I. Anderson

1615 East River Terrace,
Minneapolis 14, Minnesota.

[1] Cocconi, G., and Morrison, P., *Nature*, **184**, 844 (1959). Bracewell, R. N., *Nature*, **186**, 670 (1960).
[2] Tesla, N., *Collier's Weekly*, **26**, No. 19, 4 (1901).

FORTHCOMING EVENTS

(Meeting marked with an asterisk • is open to the public)

Monday, April 24

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London, S.W.7), at 5 p.m.—Prof. J. A. Steers and others: "Coastal Cliffs".

BRITISH NUCLEAR ENERGY CONFERENCE (at the Federation of British Industries, 21 Tothill Street, London, S.W.1), at 5.30 p.m.—Mr. A. M. Weinberg (Oak Ridge National Laboratory): "The Development of Fluid Fuel Reactors".

INSTITUTION OF ELECTRICAL ENGINEERS, LONDON GRADUATE AND STUDENT SECTION (at Savoy Place, London, W.C.2), at 6.30 p.m.—Mr. G. W. Green: "Development of City Distribution Systems".

SOCIETY OF CHEMICAL INDUSTRY, LONDON SECTION (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Prof. G. Gee, F.R.S.: "Polymer Science in the University" (Jubilee Memorial Lecture).

Tuesday, April 25

INSTITUTION OF AGRICULTURAL ENGINEERS (at the Piccadilly Hotel, London, W.1), at 10.30 a.m.—Annual General Meeting, 11.15 a.m.—Conference. 7 p.m.—Dinner.

BRITISH BIOPHYSICAL SOCIETY (in the Physics Department, Birkbeck College, Malet Street, London, W.C.1), at 11 a.m.—Scientific Papers.

INSTITUTION OF ELECTRICAL ENGINEERS, MEASUREMENT AND CONTROL SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Prof. D. M. Mackay: "Simulation of Intelligence".

SOCIETY OF CHEMICAL INDUSTRY, PLASTICS AND POLYMER GROUP (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Dr. A. S. Lodge: "The Rheology of Concentrated Polymer Solutions".

SOCIETY OF INSTRUMENT TECHNOLOGY (at Manson House, 26 Portland Place, London, W.1), at 7 p.m.—Mr. A. H. Pople: "Instrumentation in the Iron and Steel Industry".

Wednesday, April 26

ROYAL SOCIETY OF ARTS (at John Adam Street, Adelphi, London, W.C.2), at 2.30 p.m.—Sir John Cockcroft, O.M., F.R.S.: "The Training of Scientists for Industry" (Trueman Wood Lecture).

GEOLOGICAL SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 3 p.m.—Annual General Meeting. Prof. S. E. Hollingworth: "The Climatic Factor in the Geological Record" (Presidential Address).

INSTITUTION OF ELECTRICAL ENGINEERS, ELECTRONICS AND COMMUNICATIONS SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. R. H. Franklin and Mr. J. Rhodes: "Data Transmission".

CHALLENGER SOCIETY (at the Linnean Society, Burlington House, Piccadilly, London, W.1), at 5.45 p.m.—Annual General Meeting. Mr. R. L. Coet: "The Movement of Brake Bank, South of Ramsgate".

BRITISH INSTITUTION OF RADIO ENGINEERS (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6 p.m.—Symposium on "Electronic Counting Techniques".

INSTITUTION OF MECHANICAL ENGINEERS (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Annual Report of the Council.

Wednesday, April 26—Friday, April 28

BRITISH INSTITUTE OF RADIOLOGY (at the Central Hall, Westminster, London, S.W.1)—Twenty-second Annual Congress. Exhibition of Equipment and Materials used in Medical Radiology and Radiotherapy.

Thursday, April 27

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Meeting for the election of Foreign Members, followed by Mr. D. Lowe: "The National Vegetable Research Station".

ROYAL SOCIETY OF ARTS, COMMONWEALTH SECTION (joint meeting with the ROYAL COMMONWEALTH SOCIETY, at John Adam Street, Adelphi, London, W.C.2), at 5.15 p.m.—The Right Hon. The Earl De La Warr, P.C., G.B.E.: "The Work of the Commonwealth Societies".

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.15 p.m.—Prof. F. Lynen (Munich): "Biological Pathways to the Carbon Skeleton in Natural Products".• (Further lectures on May 1 and 2.)

INSTITUTION OF ELECTRICAL ENGINEERS (at Savoy Place, London, W.C.2), at 5.30 p.m.—Prof. R. F. Woolmer: "Medical Electronics" (Fifty-second Kelvin Lecture).

SOCIETY OF CHEMICAL INDUSTRY, MICROBIOLOGY GROUP (at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Annual General Meeting, followed by Mr. H. J. Bunker: "Recent Microbiological Problems in Industry".

Friday, April 28

BRITISH PSYCHOLOGICAL SOCIETY, OCCUPATIONAL PSYCHOLOGY SECTION (in the Department of Psychology, Birkbeck College, Malet Street, London, W.C.1), at 1 p.m.—Miss Lisle Klein: "Some Implications of Rationalized Production".

WORSHIPFUL SOCIETY OF APOTHECARIES OF LONDON, FACULTY OF THE HISTORY OF MEDICINE AND PHARMACY (at the Apothecaries' Hall, Black Friars Lane, Queen Victoria Street, London, E.C.4) at 4.30 p.m.—Second Annual General Meeting. 5 p.m.—Sir Geoffrey Keynes: "Timothy Bright" (Gideon de Laune Lecture).

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 9 p.m.—Mr. Edwin H. Land (U.S.A.): "Colour in the Natural Image".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

LECTURER OR ASSISTANT LECTURER IN AGRICULTURAL BOTANY—The Registrar, The University, Leeds 2 (April 28).

ASSISTANT LECTURER, Grade B, IN PHYSICS, to teach in the first instance up to General Certificate of Education "A" level, and Part 1 B.Sc. General Degree—The Clerk to the Governors, Woolwich Polytechnic, London, S.E.18 (April 29).

LECTURER (with a special interest in crop husbandry) IN THE DEPARTMENT OF AGRICULTURE—The Secretary, The University, Edinburgh (April 29).

LECTURER OR ASSISTANT LECTURER IN BACTERIOLOGY—The Registrar, The University, Leeds 2 (May 1).

LECTURER (preferably, though not necessarily, with some industrial experience and interested in teaching and research in one or more of the following fields: electrical machines; electrical power; computers, or electronics) IN ELECTRICAL ENGINEERING—The Registrar, The University, Nottingham (May 5).

READER IN APPLIED MATHEMATICS—The Clerk to the Governors, Chelsea College of Science and Technology, Manresa Road, London, S.W.3 (May 5).

ASSISTANT LECTURER (preferably with an interest in mycology) IN BOTANY—The Principal, Royal Holloway College (University of London), Englefield Green, Surrey (May 8).

ASSISTANT LECTURER OR LECTURER IN THE DEPARTMENT OF ZOOLOGY—The Registrar, The University, Liverpool 3 (May 10).

LECTURER (with a special interest in mycology, plant pathology or cognate subjects) IN BOTANY—The Secretary, The Queen's University of Belfast, Belfast 7, Northern Ireland (May 10).

PROFESSOR OF ORGANIC CHEMISTRY—The Secretary and Bursar, University College, Dublin (May 15).

ASSISTANT LECTURER IN THE DEPARTMENT OF APPLIED MATHEMATICS—The Registrar, University College of Wales, Aberystwyth (May 20).

CHAIR OF ZOOLOGY—The Registrar, University College of Wales, Aberystwyth (May 20).

FRUIT RESEARCH OFFICER (PHYSIOLOGIST) (honours graduate in science or agricultural science, or equivalent qualifications, with relevant postgraduate research experience, preferably in plant physiology or biochemistry) at the new Headquarters Laboratories of the Division of Food Preservation, C.S.I.R.O., North Ryde, Sydney, Australia, to participate in a programme of physiological and biochemical investigations to obtain a better understanding of the ripening of fruit and its behaviour in storage—Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2, quoting Appointment No. 300/298 (May 20).

LECTURER IN ZOOLOGY at Fourah Bay College (University College of Sierra Leone), to specialize in marine work—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (May 20).

SENIOR FELLOW and a SENIOR RESEARCH FELLOW (preferably with experience in elementary particle physics) IN THE DEPARTMENT OF THEORETICAL PHYSICS, Institute of Advanced Studies, Australian National University—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, May 26).

LECTURER IN BIOCHEMISTRY at the University of Western Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, May 31).

SENIOR LECTURER IN PSYCHOLOGY; and a SENIOR DEMONSTRATOR IN PSYCHOLOGY, in the Department of Psychology, School of General Studies, Australian National University, Canberra, A.C.T., Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, June 24).

ASSISTANT PROFESSOR (with a Ph.D. or equivalent, and subsequent academic, industrial or research experience) OF METALLURGY—Prof. F. A. Forward, Department of Metallurgy, University of British Columbia, Vancouver, B.C., Canada (June 30).

SENIOR LECTURER (preferably with a degree in pharmacology, physiology or biochemistry) in PHARMACOLOGY at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, June 30).

MIDDLEMASS HUNT CHAIR OF TROPICAL HYGIENE—The Registrar, The University, Liverpool (July 1).

ASSISTANT PROFESSOR (preferably with a science degree in zoology or a medical qualification) IN MICROANATOMY, to teach medical and science students and conduct research in embryology; and an ASSISTANT PROFESSOR IN GROSS ANATOMY, at Dalhousie University, Halifax, Nova Scotia, Canada—Prof. R. L. de C. H. Saunders, Canada House, Trafalgar Square, London.

LABORATORY TECHNICIAN (with a good background of hæmatological and allied laboratory technique, and preferably one "A" level science subject) IN THE RADIOISOTOPE DEPARTMENT, Victoria General Hospital, Halifax, Nova Scotia, Canada—The Nova Scotia Civil Service Commission, P.O. Box 943, Provincial Administration Building, Halifax, Nova Scotia.

LECTURER IN PHYSICS—The Secretary, Sir John Cass College, Jewry Street, London, E.C.3.

LECTURER (with a degree in chemistry or pharmacy) IN PHARMACEUTICAL CHEMISTRY; and a LECTURER (with a degree in either botany or pharmacy) IN PHARMACOGNOSY at Kumasi College of Technology,

Ghana—The Assistant Registrar, Kumasi College of Technology, 29 Tavistock Square, London, W.C.1.

Lecturer (with an M.D. or Ph.D. degree) in the Department of Physiology—Prof. M. Beznak, University of Ottawa, Ottawa, Canada.

Research Assistant in the Department of Chemistry, for the study of high pressure solubility of gases in salt solutions—Dr. Norman O. Smith, Department of Chemistry, Fordham University, New York 58, N.Y., U.S.A.

Research Associate (physics graduate, preferably with some knowledge of geology) in the Sub-Department of Geophysics of the Department of Geology, to work on some aspect of rock magnetism—The Assistant Registrar (Science), The University, Edgbaston, Birmingham 15.

Senior Lecturer (qualified to direct research) in Physics—Clerk to the Governing Body, Northern Polytechnic, Holloway, London, N.7.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Engelhard Industries, Ltd. Some Industrial Uses of Platinum Metals. Pp. 16. (London: Engelhard Industries, Ltd., 1961.) [251

Department of Scientific and Industrial Research. Fuel Research 1917–1959: a Review of the Work of the Fuel Research Organization of D.S.I.R. Pp. viii + 120 + 4 plates. (London: H.M. Stationery Office, 1960.) 15*s.* net. [251

Planning, Vol. 27, No. 448 (23 January, 1961): Parent's Views on Education. Pp. 1–32. (London: Political and Economic Planning, 1961.) 3*s.* 6*d.* [251

Ministry of Education. Selected Statistics relating to Local Education Authorities in England and Wales, Educational Year 1958–1959. Pp. ii + 25. (London: H.M. Stationery Office, 1960.) 3*s.* net. [251

Agricultural Research Council: Soil Survey Research Board. Soil Survey of Great Britain—Report No. 12, 1959. Pp. iv + 51. (London: H.M. Stationery Office, 1960.) 5*s.* net. [251

Bulletin of the British Museum (Natural History). Entomology, Vol. 10, No. 3: A Revision of Two Species Complexes in the Pyraustinae (Lepidoptera, Pyralidae), 1: *Cotachena histricalis* Walker, 2: *Syngamia floridalis* Zeller. By Paul E. S. Whalley. Pp. 96–111 + plates 3 and 4. 7*s.* 6*d.* Vol. 10, No. 4: Microlepidoptera from the Solomon Islands: Additional Records and Descriptions of Microlepidoptera collected in the Solomon Islands by the Rennell Island Expedition, 1953–54. By J. D. Bradley. Pp. 101–168 + plates 5–19. 30*s.* Vol. 10, No. 5: A Revision of the Genus *Ducetia* Stål (Orthoptera: Tettigoniidae). By D. R. Ragge. Pp. 169–208. 12*s.* Geology, Vol. 5, No. 2: Post-Ypresian Plant Remains from the Isle of Wight and the Selsey Peninsula, Sussex. By Marjorie E. J. Chandler. Pp. 13–41 + plates 4–11. 20*s.* (London: British Museum (Natural History), 1961.) [251

Research Careers in the Ministry of Aviation. Pp. 16. (London: Ministry of Aviation, 1961.) [251

Advice to a Lecturer. By Michael Faraday. Pp. 14. (London: The Royal Institution, 1961.) 2*s.* 6*d.* [251

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Imperial Chemical Industries Limited. A High Degree of Engineering. By F. B. Roberts. Pp. 24. A Degree Nearer Industry. By Kenneth Harris. Pp. 40. (London: Imperial Chemical Industries Limited, 1960 and 1961.) [251

Department of Scientific and Industrial Research: Hydraulics Research Station. Hydraulics Research Paper No. 3: Coast Erosion and Defence—Nine Questions and Answers. By R. C. H. Russell. Pp. vi + 14. (London: H.M. Stationery Office, 1960.) 1*s.* 3*d.* net. [251

General Register Office. The Registrar General's Statistical Review of England and Wales for the year 1959. Part 1: Tables, Medical. Pp. x + 331. (London: H.M. Stationery Office, 1960.) 20*s.* net. [251

This is United Steel. Pp. i + 55. (Sheffield: The United Steel Companies, Ltd., 1961.) [251

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Ministry of Agriculture, Fisheries and Food. Bulletin No. 70: Ducks and Geese. Pp. v + 93 + 8 plates. Fourth edition. (London: H.M. Stationery Office, 1960.) [251

Kodak Limited. Kodak School of Industrial and Engineering Radiography. Pp. 16. (London: Kodak Limited, 1961.) [261

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National Research Development Corporation. Report and Statement of Accounts for the year 1st July, 1959, to 30th June, 1960. Pp. ii + 30. (London: H.M. Stationery Office, 1961.) 1*s.* 6*d.* net. [261

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Ministry of Agriculture, Fisheries and Food. Fishery Investigations, Series II, Volume XXIII, No. 4: Fishing and the Stocks of Fish at Iceland. By J. A. Gulland. Pp. ii + 52. (London: H.M. Stationery Office, 1961.) 17*s.* net. [271

National Institute of Industrial Psychology. Annual Report and Statement of Accounts for the year ended 30th September, 1960. Pp. 12. (London: National Institute of Industrial Psychology, 1961.) [271

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Other Countries

United States Department of Agriculture. Farmers' Bulletin No. 2151: The Japanese Beetle: How to Control It. Pp. 16 (1 plate). (Washington, D.C.: Government Printing Office, 1960.) 15 cents.

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Indian Forest Records (New Series). Wood Preservation, Vol. 1, No. 1 (Ascu-Wood Preservative). By D. Narayanamurti and A. Purushotham. Pp. ii + 92 + 14 plates. (Delhi: Manager of Publications, 1959.) Rs. 2.35 n.p.; 4*s.* [191

Bulletin of the American Museum of Natural History, Vol. 12, Article 2: The Birds of Finca "La Selva", Costa Rica: a Tropical Wet Forest Locality. By Paul Slud. Pp. 49–148 + plates 8–26. (New York: American Museum of Natural History, 1960.) 2.75 dollars. [191

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APPOINTMENTS VACANT

THE ROYAL SOCIETY
SOPHIE FRICKE ROYAL SOCIETY RESEARCH FELLOWSHIP

Applications are invited by the Council of the Royal Society for the Sophie Fricke Royal Society Research Fellowship in the Rockefeller Institute. This is a senior research fellowship for research and study at the Rockefeller Institute in New York for a period of one year on "self chosen and self directed problems" for research in association with one or a group of scientists at the Rockefeller Institute. This Fellowship is intended "for a young man or woman of exceptional promise who has already completed graduate work, and has developed the ability to do significant research in the life sciences." It is intended that this Fellowship shall be offered "to persons who would express a firm intent not to accept subsequent employment in the United States and who desire a career in Britain and have a promising future in Britain." The field of science in which the appointment can be made for the coming academic year 1961-62 covers biophysics, biochemistry, physiology, genetics (biochemical and human), cytology (with especial emphasis on electron microscopy), histochemistry, bacteriology, virology, certain phases of organic chemistry, plant pathology, pathology and parasitology. It is intended that the holder of the Sophie Fricke Royal Society Research Fellowship for the academic year 1961-1962 should be able to travel to the United States in September or October, 1961, in order to take up appointment. An annual stipend of £3,500 or $10,000 will be provided by the Rockefeller Institute for the successful candidate, in addition to $1,000 for travel to other universities in the United States during a period of one month should that be desired and for travel to scientific meetings, and $1,000 for travel from the United Kingdom to the United States.

Applications should be made on forms to be obtained from the Assistant Secretary, the Royal Society, Burlington House, London, W.1, and should be received not later than April 30, 1961.

NORTHERN POLYTECHNIC
HOLLOWAY, LONDON, N.7

The Governing Body invites immediate applications for the following full-time appointments to commence in September next:

(a) SENIOR LECTURER IN MATHEMATICS to teach up to B.Sc. Special Degree standard. A good honours degree in mathematics is essential and postgraduate qualifications in some branch of applied mathematics would be an advantage. The successful candidate would be encouraged to engage in research. Salary scale £1,550 by £50 to £1,750, plus London allowance.

(b) ASSISTANT LECTURER IN CHEMISTRY (GRADE "B") for the teaching of organic chemistry in the degree and technical diploma courses. Industrial and some teaching experience essential. Interest in research in organo-metallic chemistry would be an advantage. Salary within scale £738 to £1,201, with additions as approved to a possible maximum of £1,486 for degree, good honours, and suitable full-time study or research. Point of entry and maximum dependent on relevant industrial or teaching experience and qualifications.

(c) ASSISTANT LECTURER IN PHYSICS (GRADE "B") to undertake teaching duties in connection with degree, diploma, and National Certificate courses. Salary scale as for (b) above.

Apply for further particulars (state appointment in which interested) and form of application.

R. H. CURRELL, F.C.A.,
Clerk.

ROYAL COLLEGE OF SCIENCE AND TECHNOLOGY
GLASGOW
(In affiliation with the University)
DEPARTMENT OF CHEMICAL TECHNOLOGY

Applications are invited for appointment as Lecturer. Applicants should have qualifications in Applied Chemistry or Chemical Engineering with experience in industry, research, or teaching. The successful applicant will be expected to teach chemical plan operation or the industrial applications of thermodynamics and physico-chemical principles, and to take an active part in research for which excellent facilities are available. Salary scale £1,050 by £50 to £1,450 by £75 to £1,850, with F.S.S.U. and family allowances.

Application forms from the Secretary of the College, George Street, C.1.

AUSTRALIA
COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION

ORGANIC CHEMIST

The Organization's Division of Plant Industry, Canberra, A.C.T., invites applications for a position as **Organic Chemist.** He is required to collaborate with a research group investigating the chemical nature and mechanism of action of growth regulators isolated from plants and he will be primarily concerned with the isolation and characterization of a naturally occurring cell division regulator.

Applicants should have a University Degree or Technical College Diploma in Organic Chemistry (or equivalent qualifications) and experience with biological systems would be an advantage.

Salary: Dependent on qualifications and experience within the ranges: £A.1,070 to £A.1,620 per annum or £A.1,620 to £A.1,950 per annum.

Salary for a woman will be £A.180 per annum less than corresponding rates for men.

Promotion within C.S.I.R.O. is by merit and may ultimately go beyond the upper limit of the range within which the original appointment is made.

Fares paid. Further particulars supplied on application to:

Mr. E. J. Drake, Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2,

to whom applications (quoting Appointment No. 130/469) should be addressed by May 20, 1961.

POST-GRADUATE TRAINING FOR STEEL MILL ENGINEERING

The British Iron and Steel Research Association and the United Steel Companies are offering to honours graduates in engineering or the physical sciences, training in Mill Research and Development, beginning September 1961.

A two-year course of varied training is envisaged, comprising an introductory course on the steel industry and its processes, practical training in the mills of some of the largest steel works in the country and with the principal plant builders, a post-graduate university course in rolling theory and allied subjects, and a special project assignment under the guidance of the staff of the leading research and development laboratories in this field.

Depending upon age and qualifications, remuneration will be £800–£850 P.A. during training, afterwards, substantive appointments within the sponsoring organisations will be offered. There is an unsatisfied and rapidly growing demand for men with good theoretical and practical grounding in this field of activity and experience indicates that they are likely to advance rapidly in an industry which offers wide scope, personal satisfaction and substantial emoluments.

Graduates under 26 and those expecting a good honours degree in 1961 are invited to write in the first instance to the Chief Development Engineer (R. & D.D.), The United Steel Companies Limited, Moorgate, Rotherham.

UNIVERSITY OF QUEENSLAND
LECTURER IN VETERINARY MEDICINE

Applications are invited for the above-mentioned position. Applicants should possess a degree in Veterinary Science from an approved University or its equivalent. The appointee should have had at least three years' postgraduate experience, including small animal practice. Salary £A.1,830 to £A.2,330 per annum. The successful applicant will enjoy the privileges of superannuation, study leave, travel grants and other benefits available to the academic staff.

Further particulars and application forms are obtainable from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on May 20, 1961.

NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING
(UNIVERSITY OF READING)

A temporary post for one year will be available from July in the Physiology Department for a recent graduate in physiology or zoology to assist with research on the bioassay of hormones in blood.

Apply, quoting ref. 61/11, to Secretary, N.I.R.D., Shinfield, Berks.

PHYSIOLOGIST, LECTURER, DEPARTMENT of Physiology, University of Ottawa, Ottawa, Canada. Applicants should have an M.D. or a Ph.D. degree. Salary up to $6,000, depending on experience. Pension plan, hospital insurance.—Applications and inquiries should be forwarded to Professor M. Beznak at the above address.

AUSTRALIA

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION

APPOINTMENT OF CHIEF

Applications are invited for appointment of **Chief** of the Organization's Division of Metrology, Sydney, N.S.W., which with the Division of Physics and Electrotechnology constitutes the National Standards Laboratory. One of the three Chiefs will act as Chairman of the National Standards Laboratory Committee which will be responsible to the Executive for the scientific policy of the Laboratory.

The Division maintains the Commonwealth standards of length, mass and associated physical quantities; conducts research in these fields and in interferometry and in vibration and develops improved methods for their determination and also provides a calibration and advisory service for industry. It also conducts research in machining and in engineering design analysis. The Division, which has extensive workshop facilities has an approximate annual budget of £A.200,000 with a total staff of 110, including 15 research officers and 15 other professional scientists.

The Chief will have considerable responsibility in framing future research policy and should have ample opportunity to carry out personal research.

Salary: £A.4,902 per annum,

Fares paid. Further particulars supplied on applications to:

Mr. E. J. Drake, Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2,

to whom applications (quoting Appointment No. 750 231) should be addressed by June 3, 1961.

SCIENTIFIC LIAISON — JAPAN

Unique opportunity for Physicist or Physical Chemist with broad scientific interests and excellent command of the Japanese language.

Major American Company has available a stimulating scientific liaison position in Japan. Strong emphasis on basic science. Period of assignment in Japan three to five years.

Reply to Box 962, T. G. Scott and Son, Ltd., 1 Clement's Inn, London, W.C.2.

CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY

MANRESA ROAD, LONDON, S.W.3

DEPARTMENT OF MATHEMATICS

Applications are invited for the post of Reader in Applied Mathematics. Salary scale: £1,800 by £50 to £2,100 per annum, plus London allowance of £38 or £51 according to age.

Information about the Department, together with further particulars of the post, may be obtained from the Clerk to the Governors. Applications by May 5, 1961.

THE EXPANDITE GROUP OF COMPANIES require qualified physicists, physical chemists and theoretical engineers to establish a new Central Research Laboratory for research in the fields of rheology, corrosion prevention, adhesives, structural joint movement stresses, and allied fields. Modern premises will provide first-class facilities, including special apparatus where necessary. Good salary and Staff Pension and Life Assurance Scheme will be available to successful applicants. —Applications in confidence, giving full details, including salary required, to Group Personnel Manager, 1-9 Chase Road, London, N.W.10.

LANCHESTER COLLEGE OF TECHNOLOGY, COVENTRY

(Principal: A. J. Richmond, B.Sc.(Eng.), Ph.D., M.I.Mech.E.)

Appointment of Additional Academic Staff

Applications invited for following posts, duties to commence September 1, 1961, or from date to be arranged

DEPARTMENT OF MECHANICAL ENGINEERING

(Head of Department: J. F. Dickenson, B.Sc. (Eng.), A.M.I.Mech.E., A.M.I.Mar.E.)

Two Senior Lecturers, one Lecturer to teach to H.N.C., H.N.D. and degree standard in Theory of Machines, Strength of Materials, Mechanics of Fluids, Thermodynamics.

DEPARTMENT OF ELECTRICAL ENGINEERING

(Head of Department: E. A. Hanney, M.Eng., Ph.D., M.I.E.E., M.Brit.I.R.E.)

One Principal Lecturer, two Senior Lecturers, one Lecturer to teach to H.N.C., Part III I.E.E. and degree standard. Opportunities exist in electronic engineering, control engineering, heavy current work and electrotechnology.

DEPARTMENT OF CHEMISTRY, METALLURGY AND TEXTILES

(Head of Department: M. E. Foss, B.Sc., Ph.D., F.R.I.C.)

One Principal Lecturer in Polymer Chemistry and Technology; one Assistant Lecturer, Grade B in Chemistry, mainly for inorganic and physical chemistry; one Lecturer in Metallurgy, mainly for Physical metallurgy; one Lecturer in Textiles, for Textile Science and Technology; to teach in H.N.C. and degree standard courses (also A.I.M. in Metallurgy and A.T.I. in Textiles).

DEPARTMENT OF APPLIED PHYSICS

(Head of Department: F. J. Pearson, B.Sc., Ph.D., A.Inst.P.)

One Senior Lecturer, one Lecturer, one Assistant Lecturer, Grade B, to teach to H.N.C. (Physics) standard and to teach Physics at various levels to engineering and science students in full- and part-time courses. The Department offers a range of postgraduate courses.

DEPARTMENT OF MATHEMATICS

(Head of Department: R. Wooldridge, M.C., B.Sc.)

Two Lecturers to teach Mathematics to H.N.C., H.N.D. and degree standard. Experience in Statistics and/or numerical analysis an advantage.

DEPARTMENT OF MANAGEMENT AND BUSINESS STUDIES

(Head of Department: W. F. Frank, Dr. Jur., B.Com., M.Sc.(Econ.), LL.B.)

One Principal Lecturer and Deputy Head of Department to act as Senior Course Tutor and organizers for the new (postgraduate) Diploma in Management Studies course. One Senior Lecturer in Economics. Four Lecturers, one specializing in Government, one in Philosophy and Politics, one in English and General Studies, one in Sociology. One Assistant Lecturer, Grade B, mainly in Accounting.

For all posts, candidates should normally hold University degree or Diploma in Technology, and, where appropriate, a professional qualification. Applicants who do not meet these requirements may be eligible by virtue of outstanding experience or other qualities. According to the nature of the post, industrial or professional experience is necessary, while some previous teaching or research experience would be an advantage.

The College is largely housed in new buildings occupied in 1960. The remaining buildings will be occupied during 1963. Equipment and general facilities in the new buildings are excellent and a real opportunity exists for the staff to take part in the many further educational developments which are projected in close and growing co-operation with industry. An outstanding feature of all Departments are many well-supported post-graduate courses of lectures. It is hoped that several Dip.Tech. courses will be offered from September, 1961.

All staff are encouraged to undertake research and/or consulting work.

Salaries (now under review): Principal Lecturers, £1,750 by £50 to £1,900 per annum; Senior Lecturers, £1,550 by £50 to £1,750 per annum; Lecturers, £1,370 by £35(4) by £40(1) to £1,550 per annum. In certain circumstances a candidate may be paid commencing salary above minimum of scale. Assistant Lecturers, Grade B, £700 to £1,150 per annum. Plus additions at the minimum and maximum for training and degree, which may amount to £285 per annum. Commencing salaries depend on age and experience.

Further particulars and application forms from the Registrar, Lanchester College of Technology, Priory Street, Coventry, to whom applications should be submitted within 12 days of the appearance of this advertisement.

W. L. CHINN,
Director of Education.

The Cooper Technical Bureau offers the opportunity to a young graduate in

ZOOLOGY · PHYSIOLOGY PHARMACOLOGY

or related subjects to join a team concerned with toxicological and pharmacological studies on new insecticides and anthelmintics. Postgraduate experience in animal physiology or biochemistry would be an advantage. Good technical facilities are available in pleasant surroundings. Salary according to age, qualifications and experience. Five day week, good recreation facilities, canteen and pension scheme.

Applications should be sent to:

The Secretary, Cooper Technical Bureau, Berkhamsted, Herts.

U.S.A. RESEARCH FOUNDATION

Applications invited for positions on the staff of a well known Research Foundation from scientists with fundamental and/or industrial research experience in:

Technical Optics
Solid State Physics
Acoustics
Plasma Physics
Nuclear Physics
Reactor Physics
Radiation Chemistry

There are openings for scientists in a number of other disciplines, both at senior and lower levels.

Infrared Tracking Project

Manager required. Ph.D. level or equivalent; electro-optical qualifications and weapon systems establishment experience.

Salaries individually negotiable in accordance with qualifications and experience.

Applications, in confidence, with date of birth, nationality, details of education, professional qualifications and experience, with dates, to **G. Hall, M.A., B.Sc., 2 and 4 Tudor Street, London, E.C.4.**

RECKITT & SONS, LIMITED

wish to appoint a Microbiologist to assist in the Bacteriological Research Laboratory.

The appointment offers a very good opportunity to a graduate, age 25 to 30, who is interested in the development of antiseptics. Some experience in the use of the Warburg apparatus would be an advantage.

The Laboratories are well-equipped and the conditions of employment are good.

Enquiries, giving full information about education, etc., should be made in writing to the Personnel Department, Reckitt and Sons Ltd., Dansom Lane, Hull.

THE PATENT OFFICE

OFFERS SCIENTISTS A CAREER WITH AN ASSURED FUTURE

SALARY. Starting salary within the scale £793 to £1,719 according to experience, with advances in the scale to £941 after two years and to £1,324 after 3 to 5 years, for those starting below these points. One promotion only (prospects excellent) raises maximum to £2,715. Further prospects up to £4,415.

QUALIFICATIONS. Age 21 to 35 and Degree or Diploma of Technology with first- or second-class honours in physics, chemistry, engineering or mathematics, or equivalent professional qualification, e.g., A.Inst.P., A.R.I.C., or corporate membership of I.C.E., I.Mech.E. or I.E.E.

INTEREST. The examination of patent specifications will maintain your knowledge of science and technology completely up-to-date and will give you inside knowledge of new manufactures well ahead of the public at large.

CONDITIONS. Location, London. Five-day week. Annual leave 4½ rising to 6 weeks with considerable freedom as to when it is utilized. Posts are permanent and pensionable (non-contributory).

Write or telephone for further information or for a visit to see the work. *The Superintending Examiner (B. Staff), The Patent Office, 25 Southampton Buildings, London, W.C.2. Holborn 8721, Ext. 324.*

AUSTRALIAN NATIONAL UNIVERSITY

INSTITUTE OF ADVANCED STUDIES
POSTS IN THEORETICAL PHYSICS

Applications are invited for appointments as Senior Fellow and Senior Research Fellow in the Department of Theoretical Physics, which is carrying out theoretical studies in nuclear physics, in the physics of elementary particles and in plasma physics. Preference will be given to applicants with experience in elementary particle physics. The present academic staff of the Department are: Professor K. J. Le Couteur, Dr. D. C. Peaslee, Dr. F. C. Barker, Dr. L. J. Tassie, Dr. B. Robson and Dr. K. Kumar. The salary range for Senior Fellows is £A.2,592 to £A.3,102. Appointment is for an initial period of five years; thereafter it may be made permanent. A Senior Fellow is entitled to one year's study leave on full pay, plus a contribution towards travel and other expenses, in every six years. The salary range for Senior Research Fellows is £A.2,272 to £A.2,752. Appointment is for three years, with possible extension to a maximum of five years. Salaries in the University are under review. Superannuation is on the F.S.S.U. pattern. Reasonable travel expenses are paid and assistance with housing is provided.

A summary of condition of appointment is available from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on May 26, 1961.

UNIVERSITY COLLEGE OF SWANSEA

DEPARTMENT OF BOTANY

Applications are invited for the following posts:

Research Demonstrator. Applicants should be graduates in Botany and will be expected to engage in research, preferably in plant physiology and biochemistry, plant pathology and ecology. Salary scale £650 to £700 per annum, together with F.S.S.U. benefits and family allowances.

Research Assistant. Applicants should be graduates in Botany or should graduate this year. The person appointed will assist the Professor in the establishment and maintenance of a Collection of plant organ and tissue cultures and in research involving these cultures. Salary in the range £500 to £650 per annum.

Further particulars can be obtained from the Registrar, University College, Singleton Park, Swansea, by whom applications (six copies), must be received not later than Saturday, May 13, 1961.

SCIENTISTS

(In Instrumentation)

required by

UNITED KINGDOM ATOMIC ENERGY AUTHORITY

at Dounreay Experimental Reactor Establishment to work with a team investigating reactor instrumentation and control problems. This work involves the study of existing systems and the development of new systems and equipment with particular regard to data reduction and presentation. Opportunities will also exist for the introduction and operation of new equipment in the Dounreay reactors.

Applicants should have at least a second-class honours degree, or equivalent, in Physics or Electrical Engineering (Electronics), and should be interested in instrumentation, particularly in the development of equipment for new methods of measurement.

Salary assessed between £790 to £1,310 according to qualifications and experience.

Rented housing and house purchase assistance available for married officers living beyond daily travelling distance.

Contributory superannuation. Hostel accommodation available.

Send post card for application form to Personnel Manager, U.K.A.E.A., E.R.E. Dounreay, Thurso, Caithness, Scotland, quoting reference 221/34.

UNIVERSITY OF LEEDS

DEPARTMENT OF EXPERIMENTAL PATHOLOGY AND CANCER RESEARCH

Applications are invited from graduates for appointment to two Research Assistantships in the Department of Experimental Pathology and Cancer Research. For the first post a graduate in chemistry or biochemistry is required to assist in the estimation of steroid and other hormones. For the second post a graduate in biological science is required to assist in the experimental study of tumour induction. The successful candidates will be eligible to apply for acceptance to work for a higher degree. Salary according to experience and qualifications.

Applications should be sent to Professor H. N. Green, Medical School, Leeds, 2.

UNIVERSITY OF LEEDS

DEPARTMENT OF AGRICULTURE

Applications are invited for appointment as Lecturer or Assistant Lecturer in Agricultural Botany at a salary on the scale £1,050 by £50 to £1,400 by £75 to £1,850 (efficiency bar at £1,550) a year for a Lecturer or within the range £800 to £950 a year for an Assistant Lecturer. Candidates should have a good honours degree in botany or agricultural botany, and have specialized in genetics and plant breeding. An interest in grassland ecology would be an advantage.

Applications (three copies), stating date of birth, qualifications and experience, together with the names of three referees, should reach the Registrar, The University, Leeds, 2 (from whom further particulars may be obtained) not later than April 28, 1961.

UNIVERSITY OF MANCHESTER

SYBIL MARY PILKINGTON FELLOWSHIP FOR RESEARCH INTO DISEASES OF THE BLOOD

Applications are invited for the Sybil Mary Pilkington Fellowship for research into Diseases of the Blood, with particular reference to the causation, treatment and cure of leukaemia in man; the research would normally be carried out in the Department of Haematology of the University in Manchester Royal Infirmary. The Fellowship is open to persons who have obtained a medical qualification registrable in the United Kingdom, the Dominions or any other country. The stipend, which is according to qualifications and experience will be within the range of £1,000 to £1,500 per annum, and the Fellowship is tenable for one year in the first instance. The Fellowship is now vacant for 1961, and the appointed Fellow would be expected to take up the Fellowship on a date to be arranged.

Applications must be sent not later than May 8, 1961, to the Registrar, the University, Manchester 13, from whom further particulars and forms of application may be obtained.

RESEARCH CHEMISTS

ICI

ORGANIC AND PHYSICAL CHEMISTS

are required by

PLANT PROTECTION LIMITED

(a subsidiary of IMPERIAL CHEMICAL INDUSTRIES LIMITED)

at its Research and Development Station

at JEALOTT'S HILL, near BRACKNELL, BERKSHIRE,

to investigate the synthesis and properties of new biologically active chemicals for use in Crop Protection. Applicants should possess good honours degrees in chemistry and postgraduate experience either at a university or in industry.

They should not exceed 30 years of age and should write in the first instance, giving brief particulars only, to the **Staff Officer, Plant Protection Limited, Fernhurst, near Haslemere, Surrey.**

British Titan Products Co Ltd

invites applications from suitably qualified or experienced

ANALYTICAL CHEMISTS

for a post in the Analytical Section of its Research Department at Billingham, Co. Durham.

Candidates should have a good degree in chemistry or an equivalent qualification. A sound knowledge of general inorganic analytical chemistry, together with some experience in modern physico-chemical methods and an interest in the development of automatic analytical techniques, is required.

The work is not routine and is concerned with the development of analytical methods for use in the Research Laboratories and the Control Laboratories. Laboratory facilities are excellent and include the latest physical instruments.

Conditions of service are considered well above average and include such benefits as a Non-Contributory Superannuation Scheme, housing, removal facilities, etc.

Further details may be obtained from:

THE PERSONNEL MANAGER,
BRITISH TITAN PRODUCTS COMPANY LIMITED,
BILLINGHAM, CO. DURHAM

Please quote reference S 8.

The Manufacturers of Brylcreem, Maclean's Toothpaste, Silvikrin and many other famous toiletry and cosmetic products require for the Product Research Laboratory

RESEARCH CHEMIST
ASSISTANT SECTION LEADER

Graduate, 20-25, for formulation and development of toiletry and cosmetic products. Similar experience useful but not essential. Working conditions are excellent, and the Company operates Profit Participation and non-contributory Pension Schemes.

Apply in writing to:

Personnel Manager,

COUNTY LABORATORIES LIMITED,

Beecham House West,
Great West Road,
Brentford, Middlesex.

RESEARCH OFFICERS

in Operational Research

Applications are invited to fill a number of vacancies in the Operational Research Department of The Steel Company of Wales Limited (Steel Division).

HONOURS GRADUATES who are stimulated by the prospect of applying scientific methods to contribute to the solution of management problems; for these positions the ability and experience of the individual are more important than the discipline of his initial degree.

MATHEMATICIANS to help form a section for the development and application of mathematical methods in operational research projects.

STATISTICIANS to join operational research teams and to supply an analytical service to other Company Departments.

COMPUTER PROGRAMMERS to join operational research teams and to supply a computing service of a very varied nature to assist research into Company computer developments on the plant as well as in the office.

There are opportunities for women graduates as mathematicians, statisticians or computer programmers.

The Department is based on Port Talbot in South Wales, but a newly established section is about to start work based on Swansea.

The conditions of work in the Company are of a high standard.

The salary offered to any individual will depend on qualifications, experience and age, but will be competitive.

Please write for application form to:

Superintendent, Personnel Services,

THE STEEL COMPANY OF WALES LIMITED

(Steel Division)

Abbey Works, Port Talbot, Glam.

LABORATORY TECHNICIAN

Required in

Rapidly expanding Radioisotope Department

VICTORIA GENERAL HOSPITAL

Halifax, Nova Scotia

QUALIFICATIONS: Good background of Hematological and Allied Laboratory Technique, preferably one "A" level science subject.

Pleasant working conditions, full Civil Service Benefits.

SALARY RANGE: Commensurate with qualifications and experience.

For further details apply to Dr. J. E. Stapleton, Radiotherapy Department, Victoria General Hospital, Halifax, Nova Scotia.

Application forms may be obtained from the Nova Scotia Civil Service Commission, P.O. Box 943, Provincial Administration Building, Halifax, Nova Scotia.

CHEMISTS IN GOVERNMENT SERVICE

A FIRST-CLASS CAREER IN RESEARCH AND DEVELOPMENT

Following are examples of vacancies at SCIENTIFIC OFFICER (£738 to £1,222) or SENIOR SCIENTIFIC OFFICER (£1,342 to £1,654) level now available:

EXPLOSIVES RESEARCH AND DEVELOPMENT ESTABLISHMENT, WALTHAM ABBEY, ESSEX—research on NOVEL ANALYTICAL TECHNIQUES involving INFRA-RED spectroscopy or CHROMATOGRAPHY (Scientific Officer).

BUILDING RESEARCH STATION, GARSTON, WATFORD, HERTS—RESEARCH on the PROPERTIES of CLAYS; their mineralogy and plasticity and the KINETICS and PHASE EQUILIBRIA of the compounds formed on heating them (Senior Scientific Officer or Scientific Officer).

CHEMICAL INSPECTORATE, WOOLWICH (and elsewhere)—RESEARCH and DEVELOPMENT on MODERN ANALYTICAL METHODS including gas chromatography, infra-red spectroscopy, radiography and differential thermal analysis (Senior Scientific Officer or Scientific Officer).

There are many other vacancies in CHEMISTRY, PHYSICS and in most other scientific disciplines. All posts carry a pension. Good promotion prospects. Full particulars from Civil Service Commission (Scientific Branch), 17 North Audley Street, London, W.1.

RESEARCH FELLOWSHIPS

R.A.E. Ministry of Aviation invites applications for a limited number of Senior and Junior Research Fellowships tenable for three years at the Royal Aircraft Establishment, Farnborough, Hants, or Bedford.

Fellows will be required to carry out Fundamental Research in connection with advanced rocket and aircraft projects. The scientific fields covered include aerodynamics, thermodynamics, aircraft and missile structures, guidance and control techniques, new synthetic polymers and their properties, electronics involving solid state physics, semi-conductors, propagation, physics and chemistry of surfaces, gas discharge physics, microwave physics, etc. Subjects will be selected according to the training and experience of the Fellows and the needs of the Establishment. Candidates must be British subjects with normally either a first- or second-class honours degree in the natural sciences, mathematics or engineering, and with evidence of a very high standard of ability in research. Exceptionally a candidate without the academic requirements but who can produce evidence of outstanding ability in research may be admitted. At least two years' postgraduate research experience required for Junior Research Fellowships (age preferably 23 to 26) and at least three years' for Senior Research Fellowships (age preferably 26 to 30).

Remuneration according to individual merit on ranges £1,325 to £1,640 (Senior Research Fellowships), £910 to £1,220 (Junior Research Fellowships). Superannuation under F.S.S.U. At expiry of a Fellowship the holder, if of suitable age, can be considered for an established (pensionable) post through a Civil Service Commission Open Competition.

Application forms and booklet obtainable from the Director, R.A.E., Farnborough, Hants, for return by April 24, 1961. Overseas candidates should send written applications, stating age, nationality and place of birth of self and parents, educational and academic qualifications, appointments held and research experience.

UNIVERSITY COLLEGE OF SWANSEA

Applications are invited from suitably qualified candidates for a Research Fellowship in Pure Mathematics. Salary within the range £800 to £1,100 per annum, according to qualifications and experience. F.S.S.U. benefits and family allowances.

Further particulars may be obtained from the Registrar, University College, Singleton Park, Swansea, by whom applications (four copies) must be received by May 13, 1961.

DIRECTOR OF RESEARCH BANANA BOARD, JAMAICA

Applications are invited for the post of Director of Research by the Banana Board, a statutory body. The Director will be expected to take charge of the Board's Research Department, which has been in operation for six years, and to direct the research programme comprehending all aspects of the banana industry from field to ship, including the control of diseases in field and storage.

Appointment will be on contract with salary according to qualifications and experience, but at a minimum of £3,000 per annum, plus appropriate allowances, leave passages, etc.

Applications should be submitted to the Secretary, Banana Board, P.O. Box 602, Kingston, Jamaica, W.I.

UNIVERSITY OF EDINBURGH
DEPARTMENT OF ELECTRICAL ENGINEERING

Applications are invited for the posts of Assistant and Lecturer in the new department of Electrical Engineering, to take up duties as soon as possible. Applicants should have a good honours degree in electrical engineering, with special interests and experience in one of the following branches: electrical machines, microwaves, plasmas, computer design techniques, solid-state electronics. New laboratories are being equipped and courses being planned which will give considerable individual responsibility to the Lecturers. Assistants would be expected to undertake research for a higher degree. Salary scales: Assistant, £800 by £50 to £950 per annum; Lecturer, £1,050 by £50 to £1,250; Bar: £1,300 by £50 to £1,400 by £75 to £1,850 per annum. Placement on the scales will be according to qualifications and experience. The posts are subject to superannuation, and family allowance is payable where applicable.

Further particulars may be obtained from the undersigned, with whom applications (six copies), giving the names of two referees, should be lodged not later than April 29, 1961.

CHARLES H. STEWART,
Secretary to the University.

UNIVERSITY OF LEEDS
DEPARTMENT OF BACTERIOLOGY

Applications are invited for appointment as Lecturer or Assistant Lecturer in Bacteriology. Salary scale for a Lecturer is £1,350 by £100 to £1,750 (efficiency bar) by £100 to £1,850 by £125 to £2,100 if medically qualified, or on the scale £1,050 by £50 to £1,400 by £75 to £1,850 (efficiency bar £1,550) if non-medically qualified; and for an Assistant Lecturer on the scale £1,050 by £50 to £1,150 if medically qualified, or on the scale £800 by £50 to £950 if non-medically qualified.

Applications (three copies), stating date of birth, qualifications and experience, together with the names of three referees, should reach the Registrar, The University, Leeds, 2 (from whom further particulars may be obtained) not later than May 1, 1961.

WYE COLLEGE
(UNIVERSITY OF LONDON)
LECTURER IN AGRICULTURAL CHEMISTRY

Applications are invited for the post of Lecturer in Agricultural Chemistry, with special reference to Animal Biochemistry and Nutrition. The appointment will be made according to qualifications and experience in the Assistant Lecturer or Lecturer grade, for which the salary scales are: Assistant Lecturer, £800 by £50 to £950; Lecturer, £1,050 by £50 to £1,400 by £75 to £1,550 (bar) by £75 to £1,850, with special London allowance £60, children's allowances and superannuation under the F.S.S.U.

Further particulars may be obtained from the Secretary, Wye College, near Ashford, Kent, to whom applications should be submitted by May 15, 1961.

RESEARCH SCIENTISTS FOR
FORMICA LIMITED

Research and Development Department

Formica Limited is a member of De La Rue—a rapidly expanding international group of companies with a reputation for leadership in a number of specialised fields.

It is intended to double the expenditure of Formica Limited upon research over the next few years during which the department will move from Tynemouth to a new research building in the South of England.

Senior qualified scientists are required for key positions in the following fields of research:

Process Chemical Engineering
Structural Plastics
Adhesion and Cohesion
Resins and Polymers

These appointments will appeal most to

CHEMICAL ENGINEERS, PHYSICAL CHEMISTS AND PHYSICISTS

but previous experience is less important than proven scientific ability.

There are vacancies also for people who expect to graduate this year.

Those who work hard and effectively can confidently expect rapid promotion and excellent remuneration. The Company encourages a broad outlook and there are frequent opportunities for travel and the exchange of views with British and foreign associates.

The publication of original papers is actively encouraged.

The starting salary for these appointments will be in the range £1,000 to £2,000.

Correspondence, which will be treated in confidence, should be addressed to:

The Research Director,
FORMICA LIMITED,
West Chirton, North Shields, Northumberland

Formica Limited—a subsidiary of The De La Rue Co. Ltd.

NASH AND THOMPSON LIMITED

a Member of the Thorn Electrical Industries Group. Research and Development Laboratories, Tolworth and Chessington, Surrey.

Radio, V.H.F. and Micro-waves; Infra-red, Light and Gamma Rays; Sub-Sonics, Acoustics and Ultra-Sonics.

A new project now commencing at the Company's Laboratories requires examination of all the known field phenomena to ascertain the perfect solution to our problem.

Applications are invited from

QUALIFIED PHYSICISTS

with a wide background and Laboratory experience, who are interested in tackling a problem where any practical solution is permitted.

Also for Physicists to undertake practical development work in conjunction with our Radio Chemistry Laboratory on the use of radio isotopes as low level power sources.

Write in the first instance to:

The Chief of Research,
Nash and Thompson Limited,
Hook Rise South, Tolworth, Surbiton, Surrey.

UNIVERSITY OF HONG KONG

SENIOR LECTURESHIP OR LECTURESHIP IN PHYSICS

Applications are invited for the above-mentioned posts, following the retirement of a Lecturer, and the expansion of the Department. Apart from teaching duties in the Department, research facilities exist for individual studies. Applicants should have postgraduate experience in research, coupled with a keen interest in teaching. The present salary scales, which are under review, are (including the allowance payable to expatriate staff): Senior Lecturer (man), £2,250 by £75 to £2,550; (woman), £1,750 by £60 to £1,990. Lecturer (man), £1,800 by £50 to £2,400; (woman) £1,425 by £40 to £1,905. The equivalent of income tax in the Colony is comparatively low. First-class sea passages are provided for expatriate staff and their families on first appointment and leaves. Accommodation at reasonable rental is provided for those receiving expatriation allowance.

Further information and particulars as to the method of application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Hong Kong and London, on May 31, 1961.

MANCHESTER COLLEGE OF SCIENCE AND TECHNOLOGY

RESEARCH ASSISTANTSHIP IN MATHEMATICS

Applications are invited from honours graduates in physics for a Research Assistantship in the Department of Mathematics. The candidate appointed would be expected to continue and develop a fundamental investigation of the rheological properties of concentrated polymer solutions. Recently developed apparatus is available for the measurement of flow birefringence and normal and shear stress components in shear flow. The work calls for initiative in the design and construction of new apparatus, and for the ability to perform series of observations of sustained accuracy. The appointment will, in the first instance, be for a period of two years at a salary of £675 for the first year rising to £700 in the second. F.S.S.U. and family allowances.

Applications should be addressed to the Registrar, The Manchester College of Science and Technology, Manchester, 1, by Saturday, April 29, 1961.

BRITISH EMPIRE CANCER CAMPAIGN

RADIATION RESEARCH

A Graduate Electrical or Electronics Engineer, age preferably 25 to 30, is required to collaborate in the development and experimental use of an electron linear accelerator, 3 cm. microwave spectroscope, and other experimental equipment which is being used to study the chemical and biological effects of microsecond pulses of radiation. Salary in accordance with qualifications and experience.

Apply in writing to the Director, Research Unit in Radiobiology, Mount Vernon Hospital, Northwood, Middlesex.

UNIVERSITY OF BIRMINGHAM

DEPARTMENT OF GEOLOGY

Applications from Physics graduates (preferably with some knowledge of Geology) are invited for a Research Associateship in the Sub-Department of Geophysics, to work on some aspect of rock magnetism. A suitably qualified candidate would be able to work for a higher degree. Initial salary within the scale £675 to £900.

Applications should be sent as early as possible to the Assistant Registrar (Science), The University, Edgbaston, Birmingham 15, from whom further particulars may be obtained.

PHYSICAL CHEMIST OR ORGANIC CHEMIST with experience of gas chromatography required for studies of trace products derived from fermentation and for the development of methods of maximum sensitivity. Salary according to age and qualifications. Non-contributory pension scheme.—Please send application in writing to the Manager, The Distillers Company Limited, Glenochil Research Station, Menstrie, Clackmannanshire, Scotland.

BIOCHEMIST. FUNDS FROM A.W.H.O. grant are available for a graduate in biochemistry or chemistry to study metabolism of insecticides in insects. Approximately £700 a year, renewable for second or third years. Opportunity for Ph.D.—Details from Dr. J. Busvine, London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, W.C.1.

UNIVERSITY OF ADELAIDE

Applications from zoologists, botanists and geneticists are invited for appointment as Demonstrator in Biology. Salary scale: £A.1,075 by £A.45 to £A.1,300. General: (a) Demonstrators are required for teaching biology to first-year students. According to their research interests demonstrators become members of staff of the Department of Zoology or the Department of Botany. (b) No provision is made for superannuation or travelling expenses, but arrangements could be made to help a candidate from the United Kingdom to secure an assisted passage under the Commonwealth Migration Scheme. (c) There are ample facilities for proceeding to higher degrees, as about half-time during term and practically full-time during vacations is available for a Demonstrator's own advanced studies and research. (d) Any further information desired will be supplied on request to the Registrar.

Applications, giving particulars of academic record and experience (if any), the names and addresses of two referees, and the time when the applicant would be free to assume duty, should be sent to the Registrar, The University of Adelaide, Adelaide, South Australia, not later than May 29, 1961.

THE INTERNATIONAL NICKEL COMPANY (MOND) LIMITED

requires a

DEVELOPMENT OFFICER

for work in connection with Chemical Products, involving the promotion of new chemical applications of nickel in fields of catalysis, co-ordination chemistry, and agriculture. Candidates, under 40 years of age, should have a sound scientific and technical training, preferably with some years practical experience in an appropriate branch of the chemical industry.

Pension and assurance schemes are in operation and, in appropriate cases, assistance can be given with housing.

Apply, giving full particulars of qualifications, experience, age, salary required, etc., to The Manager, General Division, Development and Research Department, The International Nickel Company (Mond) Limited, Thames House, Millbank, London, S.W.1. Mark envelope "Confidential D.14/N."

UNIVERSITY OF WESTERN AUSTRALIA

LECTURESHIP IN PSYCHOLOGY

Applications are invited for appointment to the above-named position in the Department of Psychology. No particular specialization is essential, but qualifications in Clinical Psychology would be an advantage for the post. The salary range for the position is £A.1,750 by £A.75 to £A.2,350 per annum, with superannuation similar to F.S.S.U. The appointee will be required to commence duties as early as possible, preferably in the near future, but the starting date will be subject to mutual agreement.

It is important that intending applicants obtain details of the procedure to be followed in applying for the post, and a copy of the Conditions of Appointment, before submitting their applications. This information is available from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on May 31, 1961.

NATIONAL COLLEGE OF FOOD TECHNOLOGY

ST. GEORGE'S AVENUE, WEYBRIDGE

Principal: J. D. Mountfield, M.Sc.Tech., Ph.D., F.R.I.C.

LECTURER IN PHYSICS

Applications are invited for the post of Lecturer in the College from graduates in physics or chemical engineering. The duties will be mainly concerned with postgraduate and four-year sandwich courses in food technology. Facilities for research are available. Salary scale: £1,370 by four at £35 and one at £40 to £1,550 per annum. Starting salary dependent on qualifications and experience.

Application forms (obtainable from the College) should be sent to the Principal as soon as possible.

UNIVERSITY OF ADELAIDE

Applications are invited for an appointment as Senior Lecturer or Lecturer in Botany (Biophysics or Morphology), depending on qualifications and experience. The University seeks a candidate who has a degree in Physics and qualifications in biophysics with some knowledge of Botany or a candidate who has a degree in Botany with qualifications in morphology and anatomy and experience of modern electron microscope techniques. The Department of Botany, in which Professor R. N. Robertson, F.R.S., will assume duties in the coming academic year, is concerned with (a) teaching Botany and Biology at first-year level; (b) teaching second- and third-year Botany courses to Science, Forestry and Agricultural Science students; and (c) postgraduate students. The Department is noted for its research in plant physiology (mineral nutrition), plant ecology (with emphasis on sclerophyllous and arid plants) and marine algal studies. Research on biochemistry and cellular physiology and on transpiration and stomatal movement will be developed under Professor Robertson. Access to an electron microscope has been arranged. There are two field stations, one at Koonamore in arid country (250 miles north of Adelaide) and the other at Keith in heath vegetation (150 miles south-east of Adelaide). Salary scales: Senior Lecturer, £A.2,450 by £A.90 to £A.2,900; Lecturer, £A.1,675 by £A.95 to £A.2,340; with provision for superannuation on the F.S.S.U. basis. The initial salary is fixed within the scale in relation to the successful candidate's qualifications and experience.

General Terms of Appointment (including details of the provision made for travelling expenses, study leave, tenure, etc.) may be had from the Registrar of the University or from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. The University Calendar may be consulted in the Library of any University which is a member of the A.U.B.C. Applications, in duplicate and giving the information listed in the last paragraph of the general terms, should be lodged with the Registrar, The University of Adelaide, Adelaide, South Australia, not later than May 31, 1961.

INDIAN INSTITUTE OF SCIENCE

BANGALORE 12 (INDIA)

Applications (six copies) on the prescribed form obtainable from the Registrar on payment of Re.1 per set by postal order, are invited for the following post at the Institute. The post is permanent with a probationary period of two years. Candidates in the service of governments, quasi-government or government-aided institutions, universities or similar institutions should send their applications through their employers. Last date for receipt of applications May 6, 1961.

Professor of Industrial Engineering and Administration in the grade Rs.1,000 by Rs.50 to Rs.1,500. Such special pay in the case of a candidate with exceptionally high qualifications and an overseas allowance not exceeding Rs.500 in the case of a foreign national as may be decided upon by the authorities of the Institute may be sanctioned. After five years of continuous service at the Institute in the grade Rs.1,000 by Rs.50 to Rs.1,500, professors are eligible for being considered for a limited number of posts in the senior scale, viz., Rs.1,600 by Rs.100 to Rs.1,800. Qualifications: High academic qualifications with industrial experience of at least ten years and ability to teach and guide work in the field of human relations, industrial planning and organization and works measurement studies. Duties: (1) To be in charge of the section of Industrial Engineering and Administration; (2) to conduct courses of study in Industrial and Production Engineering and Industrial Administration; (3) to conduct and guide research in the section and handle research problems relating to the work of the students; and (4) to be in administrative charge of the section of Economics and Social Sciences.

Further particulars can be had on request.

A. G. PAI,
Registrar.

UNIVERSITY OF LIVERPOOL

Applications are invited for the post of Assistant Lecturer or Lecturer in the Department of Zoology. The initial salary will be in the range £800 to £1,250 per annum, according to age, qualifications and experience.

Applications, stating age, academic qualifications and experience, together with the names of three referees, should be received not later than May 10, 1961, by the Registrar, The University, Liverpool, 3, from whom further particulars may be obtained, quoting Ref: C.V/N.

SCHOOL OF AGRICULTURE
KUMASI COLLEGE OF TECHNOLOGY, GHANA

Applications are invited for the following posts: (a) Lectureship in Agricultural Chemistry; (b) Lectureship in Entomology. Applicants for post (a) should have a good honours degree in Chemistry or Agricultural Chemistry with teaching and/or research experience and a definite bias for Organic Chemistry and Biochemistry. Applicants for post (b) should hold a good honours degree in Entomology or Zoology, with research or teaching experience. Postgraduate experience in a crop protection or a pest control establishment would also be a most useful qualification. The successful candidates will be required to teach students working for a four-year Diploma Course in Tropical Agriculture and will be expected to conduct research in their respective subjects. The School has available about 600 acres of land which is being developed as an experimental farm and research station, where investigations in a large range of problems are being conducted.

The Ghana Government intends to establish Kumasi College of Technology as an autonomous University in the very near future, and teaching then may be up to General Degree level. Contract appointments are normally for five years, and may be renewed. Three months' notice of resignation of an appointment is required on either side. The contract salary scale is £1,110 by £60 to £1,950 per annum. Candidates with wide experience may be appointed at Senior Lecturer level. In addition, children's allowances are paid up to a maximum of three, and a gratuity at the end of the contract at the rate of £150 for each year of satisfactory service. The entry point is fixed according to qualifications and experience. This salary scale is, however, under review. The College is fully residential, and members of staff are housed in pleasant modern bungalows on the spacious campus; climate and living conditions are good. Annual leave with three free return passages in four years is granted to members of staff and their families.

Application forms and an Information Brochure may be obtained from the Assistant Registrar, Kumasi College of Technology, 29 Tavistock Square, London, W.C.1, who will also be glad to answer any questions about these appointments.

TEA RESEARCH INSTITUTE OF EAST AFRICA
P.O. BOX 91, KERICHO, KENYA COLONY
AGRICULTURAL CHEMIST

Applications are invited for the post of Chemist. The duties of this post are: responsibility for a routine soil-testing laboratory; conducting research on tea soils and on the nutrition of the tea bush. Applicants should possess a degree in Chemistry from an approved University together with at least two years' postgraduate experience. A working knowledge of experimental statistics is essential. Salary is in the scale £1,225 by £75 to £1,750 per annum; entry point according to qualifications and experience. Free quarters with heavy furniture, or an equivalent allowance. There is a contributory Pension Scheme. Overseas leave: six months every three years or three months every two years, subject to the exigencies of the Institute's work; three weeks' local leave a year. Free passages by sea or tourist air are provided on appointment and on overseas leave for self, wife and children under fifteen years. The Institute's research station is situated in a healthy district of the Kenya Highlands, seven miles from the flourishing township of Kericho, centre of the largest tea-growing area of East Africa. Kericho has a Government European Primary School, Anglican and Roman Catholic Churches, and good shopping facilities. Further details relating to local conditions (e.g. income tax, etc.) will be supplied on request.

Applications, giving the names of two professional and one personal referee, should be sent by airmail to the Director, to arrive not later than June 1, 1961.

SOUTH-EAST ESSEX TECHNICAL COLLEGE
LONGBRIDGE ROAD, DAGENHAM

Required September, 1961. Two Lecturers in Chemistry to specialize in Inorganic or Physical Chemistry and teach to Grad.R.I.C. and B.Sc. General Standard. A good honours degree (or equivalent) essential with appropriate teaching experience. Industrial experience and/or postgraduate research desirable. Salary: £1,370 by £35(4) by £40(1) to £1,550 per annum, plus London allowance (£38 or £51).

For application form and further particulars apply to the Clerk to the Governors at the College.

UNIVERSITY OF MALAYA IN KUALA LUMPUR
DEPARTMENT OF PHYSICS

Applications are invited for posts as lecturers or assistant lecturers, depending on qualifications, in the Department of Physics, University of Malaya in Kuala Lumpur. Candidates should have a recognized Honours degree or equivalent qualification, and experience in teaching and research. The salary scale for a Lecturer is £1,148 by £49 to £1,442, £1,540 by £56 to £1,820 and for an Assistant Lecturer £1,001 by £49 to £1,099. In addition, a variable allowance is at present paid at 35 per cent of basic salary, subject to certain maxima, together with expatriation allowance at specified rates. An allowance is made towards travelling expenses and housing assistance is available.

Further particulars and application forms are obtainable from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. The closing date for the receipt of applications, in Kuala Lumpur and London, is May 15, 1961.

RESEARCH CHEMISTS
MEDICAL RESEARCH COUNCIL
GRANT AND PHYSICAL CHEMIST

Applications are invited for two posts at the British Gelatine and Glue Research Association, 2a Dalmeny Avenue, London, N.7.

1. Graduate for fundamental research on the structure and metabolism of collagen under the direction of Dr. A. Courts, in collaboration with the M.R.C.'s Rheumatism Research Unit. (Grant from the Medical Research Council.)
2. Physical Chemist, preferably with several years of postgraduate experience, for fundamental studies on gelation.

Salaries will be in accordance with qualifications and experience. It is possible that, in Post 1, the holder will have the opportunity to obtain a higher degree.

Applications to the Director of Research by May 23, 1961.

ESSEX
MID-ESSEX TECHNICAL COLLEGE AND SCHOOL OF ART
MARKET ROAD, CHELMSFORD

Applications are invited for the following posts from September, 1961, unless otherwise stated:

SCIENCE DEPARTMENT

(1) Lecturer in Inorganic or Physical Chemistry to teach up to H.N.C. and B.Sc. (General) Degree level. Applicants should have a good honours or higher degree, with appropriate teaching and/or research and/or industrial experience.

(2) Assistant Grade B for Mathematics to teach mainly O.N.C. and G.C.E. ("A" and "O" levels), but more advanced work would be available to a suitable applicant. An honours degree and teaching or industrial experience are desirable. An interest in the teaching of Statistics would be an additional recommendation.

Salaries: Lecturer, £1,370 rising by annual increments of £35 (4) and one of £40 to a maximum of £1,550 per annum. Assistant Grade B, £700 per annum rising to £1,150 per annum (plus additions for training and graduate qualifications if in accordance with the Burnham Further Education Report, 1959).

Details and forms from Clerk to the Governors, to whom completed forms should be returned as soon as possible.

NATIONAL COLLEGE OF FOOD TECHNOLOGY
ST. GEORGE'S AVENUE, WEYBRIDGE
Principal: J. D. Mountfield, M.Sc.Tech., Ph.D., F.R.I.C.

LECTURER IN CHEMISTRY

Applications are invited for the post of Lecturer in the College from graduates in Chemistry or Biochemistry. The duties will be mainly concerned with postgraduate and four-year sandwich courses in food technology. Facilities for research are available. Salary scale: £1,370 by four at £35 and one at £40 to £1,550 per annum. Starting salary dependent on qualifications and experience.

Application forms (obtainable from the College) should be sent to the Principal as soon as possible.

SCHOOL OF PHARMACY
KUMASI COLLEGE OF TECHNOLOGY, GHANA

Applications are invited for the following posts: (a) Lecturer in Pharmaceutical Chemistry; (b) Lecturer in Pharmacognosy. Applicants for post (a) should hold a degree in Chemistry or Pharmacy; for post (b) a degree in either Botany or Pharmacy. In both cases the applicant should be eligible for registration as a pharmacist in Great Britain. The successful candidates will be expected to teach up to the standard of the Qualifying Examination of the Pharmaceutical Society of Great Britain.

The Ghana Government intends to establish Kumasi College of Technology as an autonomous University in the very near future, and teaching may then be up to General Degree level. In addition to teaching duties, the candidates will be expected to participate in a Research Programme of Investigation of the Medicinal and Toxic Plants of the Country. This programme is being carried out in conjunction with Chelsea College of Science and Technology.

Contract appointments are normally for five years, and may be renewed. Three months' notice of resignation of an appointment is required on either side. The contract salary scale is £1,063 15s. by £57 10s. to £1,868 15s. The entry point is fixed according to qualifications and experience. This salary scale is now under review. In addition, children's allowances are paid up to a maximum of three, and a gratuity at the end of the contract at the rate of £150 for each year of satisfactory service. The College is fully residential and members of staff are housed in pleasant modern bungalows on the spacious campus; climate and living conditions are good. Annual leave with three free return passages in four years is granted to members of staff and their families.

Application forms and an Information Brochure may be obtained from the Assistant Registrar, Kumasi College of Technology, 29 Tavistock Square, London, W.C.1, who will also be glad to answer any questions, either about the work of the School or about living conditions in Ghana.

UNIVERSITY OF SYDNEY
SENIOR LECTURESHIP IN PHARMACOLOGY

Applications are invited for the above-mentioned position. Preference will be given to candidates with a degree in Pharmacology, Physiology or Biochemistry and with postgraduate research experience. A first-degree in Pharmacy is also desirable. The salary for a Senior Lecturer is within the range £A.2,550 by £A.95 to £A.3,000 per annum, plus cost of living adjustments (at present £A.36 per annum), and will be subject to deductions under the State Superannuation Act. The commencing salary will be fixed according to the qualifications and experience of the successful applicant. Under the Staff Members' Housing Scheme in cases approved by the University and its Bankers, married men may be assisted by loans to purchase a house.

Further particulars and information as to the method of application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on June 30, 1961.

UNIVERSITY OF EDINBURGH
DEPARTMENT OF BOTANY

Applications are invited for appointment of two Research Assistants in Plant Taxonomy to collaborate in compiling a flora of Turkey. Applicants should have a Ph.D. or suitable taxonomic experience. The appointments are for a period of three years, and the salary scale is £650 by £50 to £950 per annum, plus a travel allowance of £50 a year.

For further information apply to Dr. P. H. Davis, University Department, at Royal Botanic Garden, Edinburgh, 3, with whom applications should be lodged as soon as possible.

CHARLES H. STEWART,
Secretary to the University.

QUEEN'S UNIVERSITY
KINGSTON, ONTARIO, CANADA
LECTURER IN CHEMISTRY

Applications are invited for the above post. Candidates should have research experience. The appointee will be expected to teach undergraduates and carry on fundamental research. The appointment is probationary for the first two years.

Applications should include names of two referees to whom application may be made for references. Details of papers published and research interests should also be given. Further particulars can be obtained from Professor J. K. N. Jones.

BRIGHTON EDUCATION COMMITTEE

BRIGHTON TECHNICAL COLLEGE

Principal: G. E. Watts, C.B.E., M.A., Ph.D. (Cantab), B.Sc. (Lond.), F.R.I.C.

Required for September 1, 1961. Lecturer and Assistant Lecturers (Grade B) (2) in Physics. Applicants should possess honours degree or honours dip.tech. in applied physics, and preferably have had teaching experience. Industrial and/or research experience in applied physics desirable for all posts. Lecturer in Physical chemistry with good honours degree and teaching experience to teach to degree and Grad.R.I.C. levels. Suitable research or industrial experience an advantage. Salaries: Lecturer, £1,370 by £35 (4) by £40 to £1,550; Assistant Lecturer (Grade B), £700 by £27 10s. to £1,150, plus training and graduate allowances if appropriate. Increments may be allowed in either scale for approved experience.

Further particulars and forms of application from the undersigned, to be returned to the Principal, Brighton Technical College, Richmond Terrace, Brighton 7, within ten days.

W. G. STONE,
Director of Education.

54 Old Steine,
Brighton.

JAMAICA COLLEGE OF ARTS, SCIENCE AND TECHNOLOGY

KINGSTON

Principal: H. Falkner, M.Sc.(Wales), B.Sc. (Lond.), A.Inst.P.

Applications are invited for a Senior Lecturer in Pharmacy in the Science Department. Salary scale: £1,500 by £50 to £1,700 per annum, plus marriage allowance for men of £100 per annum. Entry point according to qualifications and experience. Appointment may be either permanent or on contract. Possible housing assistance. The College is a rapidly developing one.

Further information obtainable from Council for Overseas Colleges, 12 Lincoln's Inn Fields, London, W.C.2, to whom applications (six copies), giving age, qualifications, experience and names of three referees, should be sent by May 12, 1961.

UNIVERSITY OF GLASGOW

DEPARTMENT OF GENETICS

Applications are invited for the post of Research Assistant (part-time or full-time). Work will include diverse aspects of the handling of research data in human genetics. Previous experience not essential. Commencing salary (full-time) £400 to £750 per annum, according to qualifications.

Applications (three copies) should be lodged, not later than April 29, 1961, with the Secretary of the University Court, The University, Glasgow, W.2.

ROBT. T. HUTCHESON,
Secretary of University Court.

UNIVERSITY OF DURHAM

THE MEDICAL SCHOOL, KING'S COLLEGE, NEWCASTLE UPON TYNE

Applications are invited for the post of Motion Picture and T.V. Assistant in the Department of Photography in the Medical School. Applicants should have considerable experience in sound and electronics and be able to operate a camera and edit. As the successful applicant will work with modern equipment and facilities producing teaching and research films in an expanding field of medicine, pure and applied science, pioneering and hard work are involved. Appointment will be made on the Technicians Grade £490 to £675 or on the Senior Technicians Grade £690 to £815, according to qualifications and experience.

Applications, giving full details, should be sent as soon as possible to Mr. C. J. Duncan, The Director, Department of Photography.

GLASSBLOWERS. FIRST-CLASS GLASSblowers required to make Laboratory glassware, mostly intricate "specials." The jobs will appeal particularly to glassblowers with a lively interest in producing "one-offs" to drawings rather than in mass production. A high degree of manipulative skill is essential; experience in lathe work is desirable. Staff appointment basic salary £900 per annum; with overtime, total earnings can reach £1,150 per annum. Opportunities for advancement. 42-hour five-day week. Pension scheme and other benefits in keeping with the policies of our Parent Company, Fisons Limited. Ideal working conditions in a brand new factory which includes modern canteen. Assistance with removal expenses.—Send full details to the Works Manager, Loughborough Glass Company Ltd., Loughborough, Leicestershire.

OPPORTUNITIES FOR SCIENCE AND MATHEMATICS GRADUATES TO TAKE UP TEACHING

Graduates in Science and Mathematics who are having second thoughts about the careers they chose after leaving the university, or married women with degrees in these subjects who would like to teach full- or part-time should write to the Chief Education Officer (Dept. N2), County Offices, Chelmsford, Essex, for particulars of a brief training scheme to make it easier for them to take up teaching.

If accepted for service in Essex schools, they can be given a short course of training and teaching practice before they take up regular teaching posts. From the start of the course they will be paid at full Burnham rates, with any additional increments to which their previous employment may entitle them.

THE MANCHESTER COLLEGE OF SCIENCE & TECHNOLOGY

(Faculty of Technology in the University of Manchester)

Appointment of

LECTURERS IN ELECTRICAL ENGINEERING

Applications are invited for Lectureships in Electrical Engineering with equivalent status in the University of Manchester.

Salary will be in the scale £1,050 by £50 to £1,400 by £75 to £1,850 with family allowances and F.S.S.U.

The conditions of appointment and form of application may be obtained from the Registrar, The Manchester College of Science and Technology, Manchester, 1. The last date for the receipt of applications is May 12, 1961.

SOUTH-WEST ESSEX TECHNICAL COLLEGE AND SCHOOL OF ART

FOREST ROAD, WALTHAMSTOW, E.17

PHYSICAL-BIOCHEMISTRY RESEARCH

Honours Graduates (Special or General) and students in their Final Year are invited to apply for appointment as Research Assistants in Physical Biochemistry. Research Assistants prepare for higher Degrees (M.Sc. or Ph.D.) or for the Diploma of the Royal Institute of Chemistry. The following fields are covered: Reactions of DNA and RNA and nucleic acid components with formaldehyde and aminoacids; Biosynthesis of proteins; Reactions of disulphide groups with ascorbic acid and aminoacid-aldose complexes; Reduction of Redox compounds by aminoacid-aldose complexes; Reaction of aminoacids and proteins with steroids or with phosphoaldoses; Protein and biological cell electrophoresis; Effect of diet and blood pH on genetic ratios. The work involves correlation of the results of several manual and recording physico-chemical tools: viz. Absorption spectrophotometry; pH, Redox and polarographic determinations; moving boundary and high-voltage paper electrophoresis; Ion exchange; Paper and Vapour Phase Chromatography. Basic salary £400 per annum, plus supplementary payment for part-time teaching, bringing the total annual salary to approximately £600.

Further details may be obtained from the Principal.

UNIVERSITY OF MALAYA IN KUALA LUMPUR

DEPARTMENT OF BOTANY

Applications are invited for the post of Lecturer or Assistant Lecturer, according to qualifications in the Department of Botany, University of Malaya in Kuala Lumpur. The post is available now. Candidates should have a recognized degree or equivalent, and experience in teaching and research in plant physiology or cryptogamic botany. The salary scale for a Lecturer is £1,148 by £49 to £1,442/£1,540 by £56 to £1,820 and for an Assistant Lecturer £1,001 by £49 to £1,099. In addition, a variable allowance is at present paid at 35 per cent of basic salary, subject to certain maxima, together with expatriation allowance at specified rates. An allowance is made towards travelling expenses and housing assistance is available.

Further particulars and application forms are obtainable from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. The closing date for receipt of applications, in Kuala Lumpur and London, is May 31, 1961.

AUSTRALIA

UNIVERSITY OF NEW SOUTH WALES NEWCASTLE UNIVERSITY COLLEGE

LECTURER—DEPARTMENT OF CHEMISTRY

Applications are invited for appointment to the position of Lecturer in Chemistry at Newcastle University College. The Department of Chemistry has a staff of one Associate Professor and nine lecturers and senior lecturers, and provides courses at the pass degree and honours degree level. There are a number of students proceeding to higher degrees. The successful applicant will be required to lecture in analytical chemistry. Applicants should possess an honours degree in chemistry and preferably a higher degree. Experience and special interest in modern physical methods are also required. Salary: £A.1,766 range £A.2,471 per annum. Commencing salary is determined by qualifications and experience. Successful applicant will be eligible, subject to passing a medical examination, to contribute to the State Superannuation Fund. First-class ship fares to Sydney of appointee and his family will be paid.

Four copies of applications, including the names of two referees, should be lodged with the Agent General for New South Wales, 56 Strand, London, W.C.2, and a copy forwarded by airmail to the Appointments Section, University of New South Wales, Box 1, Post Office, Kensington, N.S.W., Australia, before June 9, 1961. Applicants outside the United Kingdom and Eire need only submit one copy of their application to the London address in addition to that sent to Sydney.

UNIVERSITY OF QUEENSLAND

LECTURER IN ANIMAL HUSBANDRY

Applications are invited for the above-mentioned position. The department proposes to expand and develop work already in progress in the fields of meat production and re-production, and invites applications for a lectureship in either of these two fields. In the field of meat production preference will be given to a candidate with knowledge of growth process in relation to body composition, carcase appraisal, and metabolism. Previous experience in the Meat Industry would be valuable. In the field of reproduction, the applicant will be expected to lecture and to research in fertility and reproduction in sheep or cattle or in artificial insemination, with special reference to cattle and pigs. Experience in these subjects is desirable, but consideration will be given to applicants with an advanced basic background of nutrition, physiology or biochemistry. Salary £A.1,830 to £A.2,330 per annum. The successful applicant will enjoy the privileges of superannuation, study leave, travel grants and other benefits available to the academic staff.

Further particulars and application forms are obtainable from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on May 31, 1961.

MANCHESTER COLLEGE OF SCIENCE AND TECHNOLOGY

(Faculty of Technology in the University of Manchester)

Applications are invited for a Lectureship in Biochemistry in the College with the title and status of Lecturer in the University of Manchester. Preference will be given to candidates with an interest in Physical Biochemistry or the study of enzymes and their mechanisms. Salary: According to qualifications and experience on scale £1,050 by £50 to £1,400 by £75 to £1,850 per annum. Superannuation under the F.S.S.U. Family allowances.

Conditions of appointment and form of application may be obtained from the Registrar, The Manchester College of Science and Technology, Manchester, 1. The last day for the receipt of applications is Saturday, May 6, 1961.

NATIONAL COLLEGE OF FOOD TECHNOLOGY

ST. GEORGE'S AVENUE, WEYBRIDGE

Principal: J. D. Mountfield, M.Sc.Tech., Ph.D., F.R.I.C.

ASSISTANT LECTURESHIPS

Applications are invited for Assistant Lectureships in the College from graduates in (a) Chemistry or Biochemistry, (b) Microbiology, (c) Physics or Engineering. Facilities for research are available. Salary scale: £790 by fifteen at £27 10s. and one at £37 10s. to £1,240 per annum. Starting salaries dependent on qualifications and experience.

Application forms (obtainable from the College) should be sent to the Principal as soon as possible.

BIRKENHEAD EDUCATION COMMITTEE

BIRKENHEAD TECHNICAL COLLEGE

Principal: C. V. Vinten Fenton, M.Sc., A.M.I.Mech.E., A.M.I.E.E.

Applications are invited for the following vacancies:

SCIENCE DEPARTMENT

Senior Lecturer in Physical Chemistry. Lecturer in Physical or Inorganic Chemistry. Assistant Grade "B" in Physics. Assistant Grade "A" in Chemistry. Salary in accordance with the Burnham Technical Report, 1959.

Further particulars and forms of application may be obtained from the undersigned, to whom completed applications should be returned by May 1, 1961.

H. GLYN WILKINSON,
Director of Education.

63 Hamilton Square,
Birkenhead.

NORTH OF SCOTLAND COLLEGE OF AGRICULTURE

The Governors invite applications for the temporary post of Assistant Advisory Officer in Mycology. Candidates should possess an honours degree in botany or agricultural botany, and should have specialized in plant pathology. The post will last for a period of five to six months. Salary scale: Grade III (National), £1,004 to £1,578 per annum; Grade IVa (National), £718 to £993 per annum; Grade IVb (National), £718 to £963 per annum. Entry to the above scales will be according to age, qualifications and experience. Medical examination.

Forms of application, which may be obtained from the Secretary of the College, 413 Union Street, Aberdeen, must be lodged not later than May 3, 1961.

DEVON EDUCATION COMMITTEE

DEVON EDUCATION COMMITTEE AND THE HERBERT WHITLEY SCIENTIFIC AND EDUCATIONAL TRUST

Applications are invited for the post of Education Officer for the Herbert Whitley Scientific and Educational Trust, with headquarters at the Paignton Zoological and Botanical Gardens. Applicants, preferably graduates, should have wide biological interests. An attractive and unusual post dealing with children and students, with opportunities for research.

Full particulars from the Chief Education Officer, County Education Office, Larkbeare, Topsham Road, Exeter. Last date for the receipt of applications May 13, 1961. S.a.e. (foolscap) required.

UNIVERSITY COLLEGE OF WALES ABERYSTWYTH

Applications are invited for the post of Assistant Lecturer in the Department of Applied Mathematics, to take up duties on October 1, 1961.

Further particulars and forms of application can be obtained from the Registrar, to whom applications should be sent not later than May 20, 1961.

UNIVERSITY OF GLASGOW

DEPARTMENT OF GENETICS

Applications are invited for the post of Blood-Group Serologist to take part in a search for genetical linkages in man. Commencing salary £1,200 per annum.

Applications (three copies) should be lodged, not later than April 29, 1961, with the Secretary of the University Court, The University, Glasgow, W.2.

ROBT. T. HUTCHESON,
Secretary of University Court.

INSTITUTE OF CANCER RESEARCH: Royal Cancer Hospital. Research Assistant required in the Chester Beatty Research Institute, Fulham Road, S.W.3, for work on protein structure and other studies of a biophysical character. Graduate in physics for physical chemistry) preferred, but non-graduate with suitable qualifications and experience might be considered. Salary on M.R.C. scales for Technical Officers.—Applications, with names of two referees, to the Secretary, 33 Sumner Place, S.W.7, quoting ref. 301/B/60.

TECHNICIAN REQUIRED FOR RESEARCH Department of Immunology. Biochemical experience desirable. Whitley scales, superannuation under F.S.S.U. Holiday arrangements will be honoured.—Applications, giving full details of experience, etc., should be addressed to the Secretary, Wright-Fleming Institute, St. Mary's Hospital Medical School, Paddington, W.2, to reach him not later than May 1, 1961.

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE

Physicist, Engineer, or Biological Scientist with interest and experience in instrument development required to work with the Professor of Epidemiology on problems connected with the measurement of environmental and physiological variables in population groups. Appointment for two years in first instance. Successful applicant will be seconded to the Bio-Engineering Laboratory of the Division of Human Physiology, National Institute of Medical Research. Salary scale £800 to £1,000, depending on age and experience. Appointment to start June, 1961.

Applications to the Dean, London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.

CHEMIST

A leading food manufacturing Company wish to appoint a Chemist to the staff of their new Product Development Group.

The Chemist appointed will be concerned with the development of canned products. Candidates aged not over 35 years, must have full knowledge of canning technology. The Company's premises are situated in the West London area.

Applicants are asked to write giving full details of age, education, qualifications and experience to Box No. G8808, c/o Whites, 72 Fleet Street, London, E.C.4.

NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING

(UNIVERSITY OF READING)

BIOMETRICIAN

Graduate with mathematical and biological interests required in the Section of Statistics. Duties invcive consultation and research on design and analysis of experiments for which a knowledge of statistics is desirable, though not initially essential as training will be given. Appointment in Scientific Officer (£717 to £1,222) or Senior Scientific Officer (£1,302 to £1,654) grade, according to age and experience.

Applications, naming two referees, to Secretary, N.I.R.D., Shinfield, Reading. Quote ref. 61/12.

ONTARIO CANCER FOUNDATION

HAMILTON CLINIC
HAMILTON GENERAL HOSPITAL,
HAMILTON, ONTARIO

Applications are invited for appointment as Clinical Physicist. Applicants should possess at least an honours degree in physics or equivalent. Some experience in hospital physics is desirable but not necessary. An interest in research in clinical physics or radiobiology is expected. Minimum initial salary for untrained honours graduate is $5,000 per annum; pension scheme.

Applications should be sent to the undersigned, from whom further details may be obtained.

R. J. HORSLEY,
Senior Physicist.

FORDHAM UNIVERSITY

NEW YORK CITY
DEPARTMENT OF CHEMISTRY
RESEARCH ASSISTANTSHIP

For the study of high pressure solubility of gases in salt solutions. Geochemical implications. Prefer student working toward the Ph.D. $200/month.

Apply to: Dr. Norman O. Smith
Department of Chemistry
Fordham University
New York 58, N.Y., U.S.A.

LAC RESEARCH FELLOWSHIP

A chemist with a good degree and research experience, preferably in polymers or surface coatings, is required for a special research project on Indian lac, involving basic studies of chemical modifications and initial evaluation of their technical potentialities. The salary will be fully commensurate with age and experience.

Applications, with the names of two referees, should be sent to the Directors, Paint Research Station, Waldegrave Road, Teddington, Middlesex.

UNIVERSITY COLLEGE OF WALES ABERYSTWYTH

DEPARTMENT OF ZOOLOGY

Applications are invited for the Chair of Zoology at a commencing salary of not less than £2,600 per annum.

Further particulars can be obtained from the Registrar. Ten copies of applications, together with the names of three referees, should be sent by May 20, 1961.

T. MAELGWYN DAVIES,
Registrar.

UNIVERSITY OF NATAL

DEPARTMENT OF PHYSICS

Applications are invited from suitably qualified persons for appointment to the post of Senior Lecturer in Physics, Durban. The salary scale attached to the post is R.3,180 by R.120 to R.4,140 per annum. (£1,590 by £60 to £2,070.) The commencing notch on this scale will be dependent on the qualifications and/or experience of the successful candidate. The University reserves the right to appoint someone other than from those who make application.

Application forms and further particulars are obtainable from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in South Africa and London, on May 31, 1961.

FOURAH BAY COLLEGE

UNIVERSITY COLLEGE OF SIERRA LEONE

Applications are invited for a Lectureship in Zoology to specialize in marine work. Salary scale: £965 by £50 to £1,415; £1,490 by £75 to £1,790 per annum, entry point according to qualifications and experience. Negotiations in progress for salary revision. F.S.S.U. Outfit and family allowance (maximum £300). Passages on appointment, annual leave and normal termination. Part-furnished accommodation at reasonable rent.

Detailed applications (six copies), naming three referees, by May 20, 1961, to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

SIR JOHN CASS COLLEGE

JEWRY STREET, LONDON, E.C.3

DEPARTMENT OF PHYSICS

The Governors invite applications for the post of Lecturer in Physics. Candidates are expected to have qualifications and experience enabling them to take an effective part in the work of preparing students for Special and General degrees of the University of London. Ability to undertake research is desirable. The appointment will date from September 1, 1961, or as soon as possible thereafter. Salary scale: £1,408 by £35 to £1,601.

Further particulars and form of application may be obtained from the Secretary.

MANCHESTER COLLEGE OF SCIENCE AND TECHNOLOGY

(FACULTY OF TECHNOLOGY IN THE UNIVERSITY OF MANCHESTER)

Applications are invited for a Demonstratorship and a Research Assistantship in the Department of Biochemistry. Candidates with appropriate qualifications will be able to study for higher degrees. Salary: £675 by £25 to £700. Superannuation under the F.S.S.U. Family allowances.

A form of application may be obtained from the Registrar, The Manchester College of Science and Technology, Manchester, 1. The last day for the receipt of applications is Saturday, May 6, 1961.

UNIVERSITY OF ABERDEEN

NATURAL PHILOSOPHY DEPARTMENT

Applications invited for Lectureships and Assistantships in Experimental Physics, Theoretical Physics and Electronics. Salaries: Lecturers, £1,050 by £50 to £1,400 (Bar) by £75 to £1,850; Assistants, £800 by £50 to £950, with F.S.S.U., child allowance and part removal expenses. Initial placings according to qualifications and experience.

Particulars and forms of application from the Secretary, The University, Aberdeen, with whom applications (eight copies) should be lodged by May 15, 1961. Applicants outside the British Isles may submit one copy of application.

TECHNICAL INFORMATION SERVICE. Aslib has two vacancies for literature searchers to handle wide range of technical inquiries. First, salary up to £1,000, requires experience of this type of work and involves supervision of small team of searchers. Second, salary up to £700, might suit young science graduate attracted by work with technical literature.—Apply Director, Aslib, 3 Belgrave Square, London, S.W.1.

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